INCONTRO DI AGGIORNAMENTO
SUI **DISORDINI LINFOPROLIFERATIVI**
E SUI PROTOCOLLI
DELLA **FONDAZIONE ITALIANA LINFOMI**

Torino, 14 dicembre 2018

Update sul linfoma mantellare

Inquadramento istopatologico

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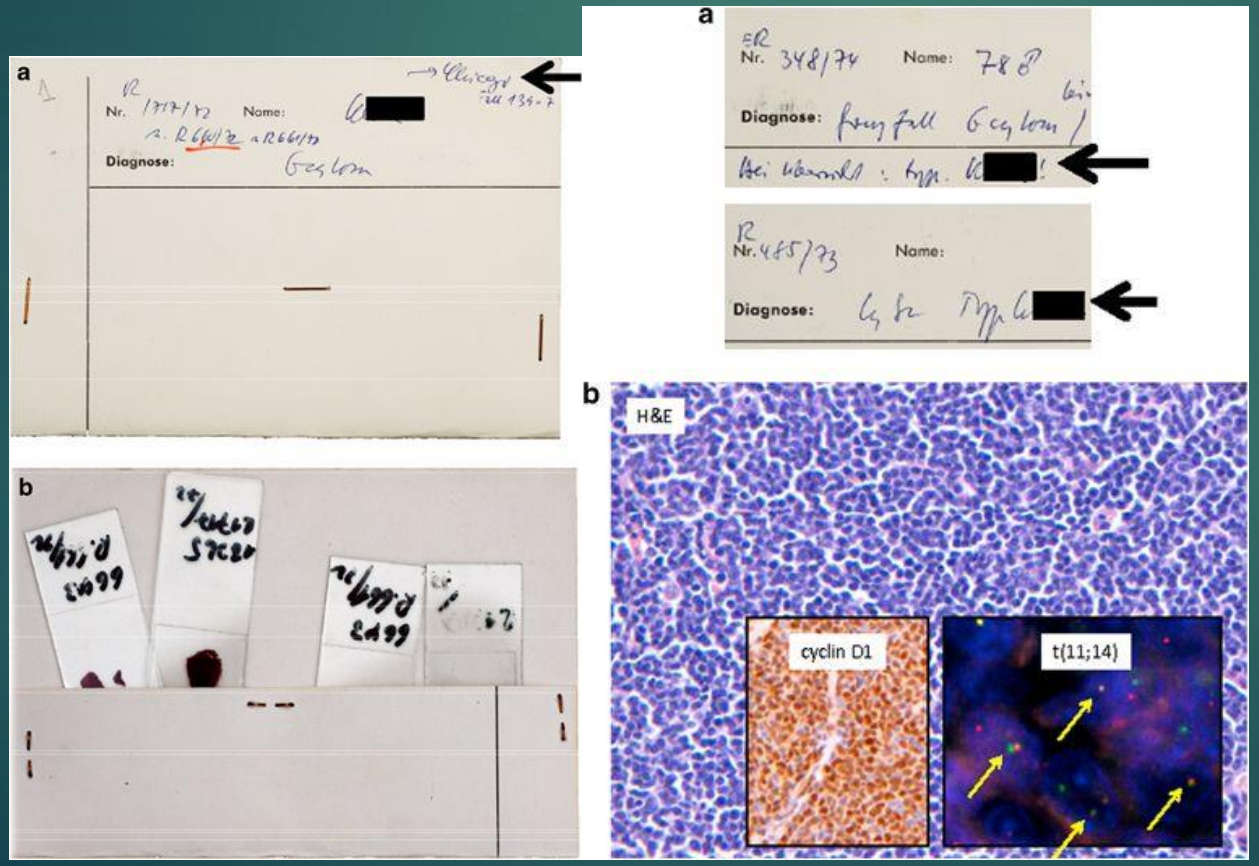
Anatomia Patologica 1U, AOU Città della Salute e della Scienza

Linfoma a cellule del mantello

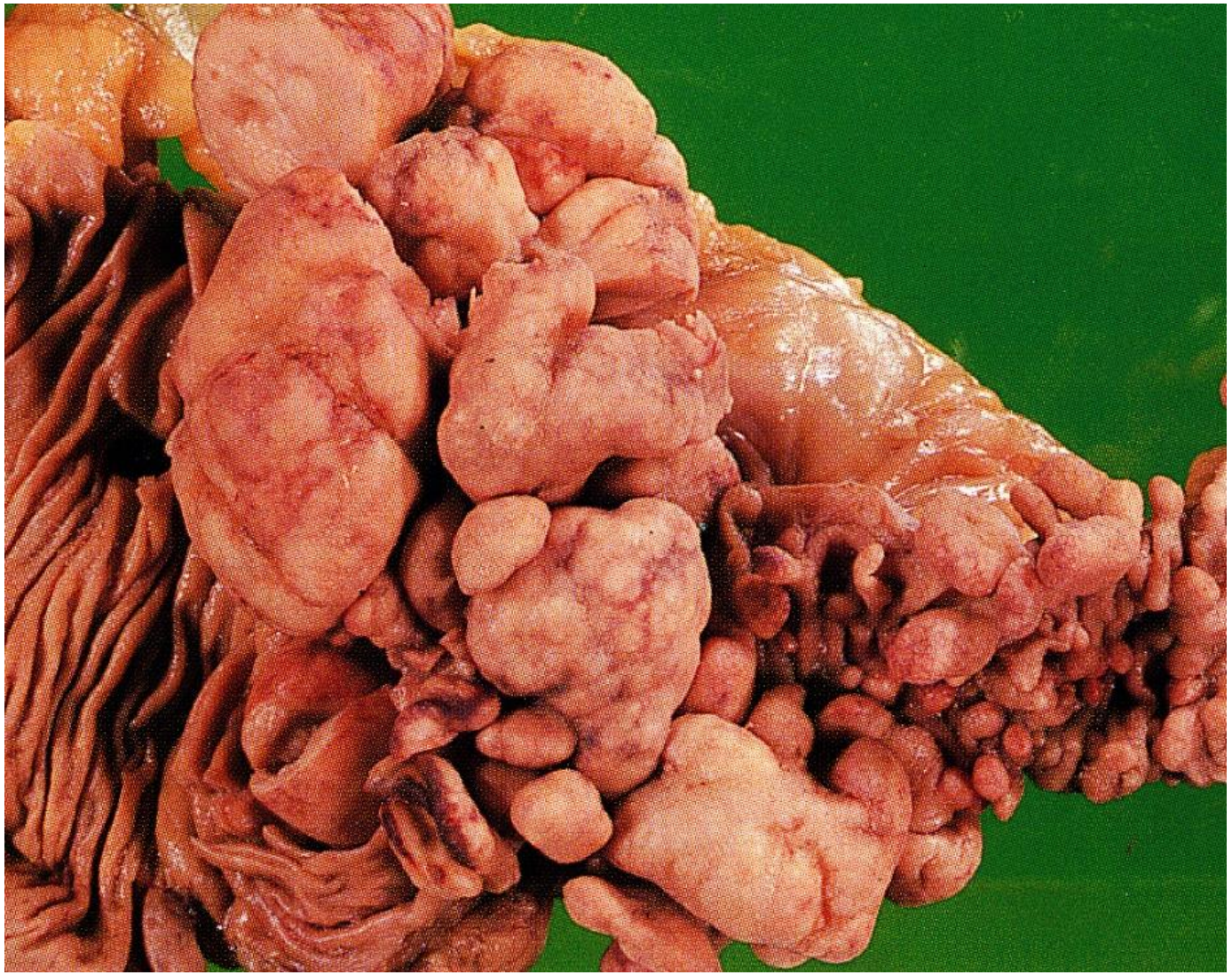
- Verosimilmente identificato da Lennert nel 1972 come «type K» e alla fine come «centrocitico»



Klapper *et al. Leukemia* **volume27**, 519–521 (2013)

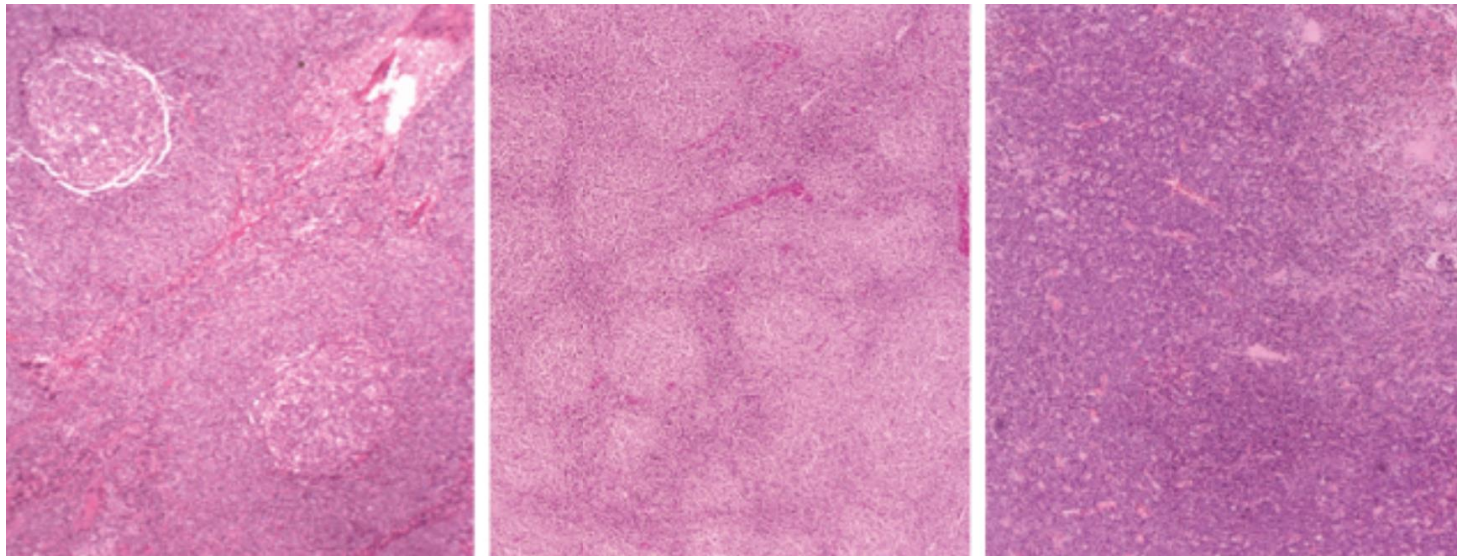
Macroscopia

Unico aspetto caratteristico (ma non specifico) il quadro di poliposi linfomatoide

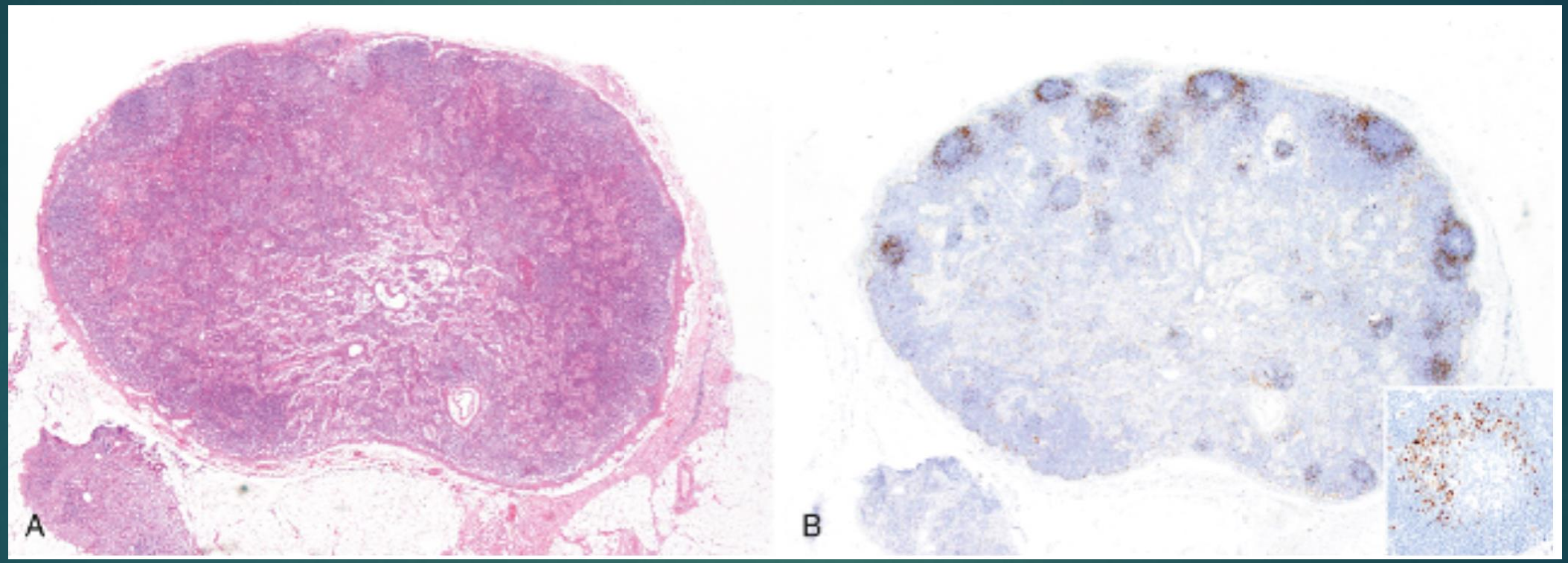


Microscopia: pattern architetturali

- Neoplasia in situ <<<
- Mantellare <<
- Nodulare <<
- Diffuso >>>

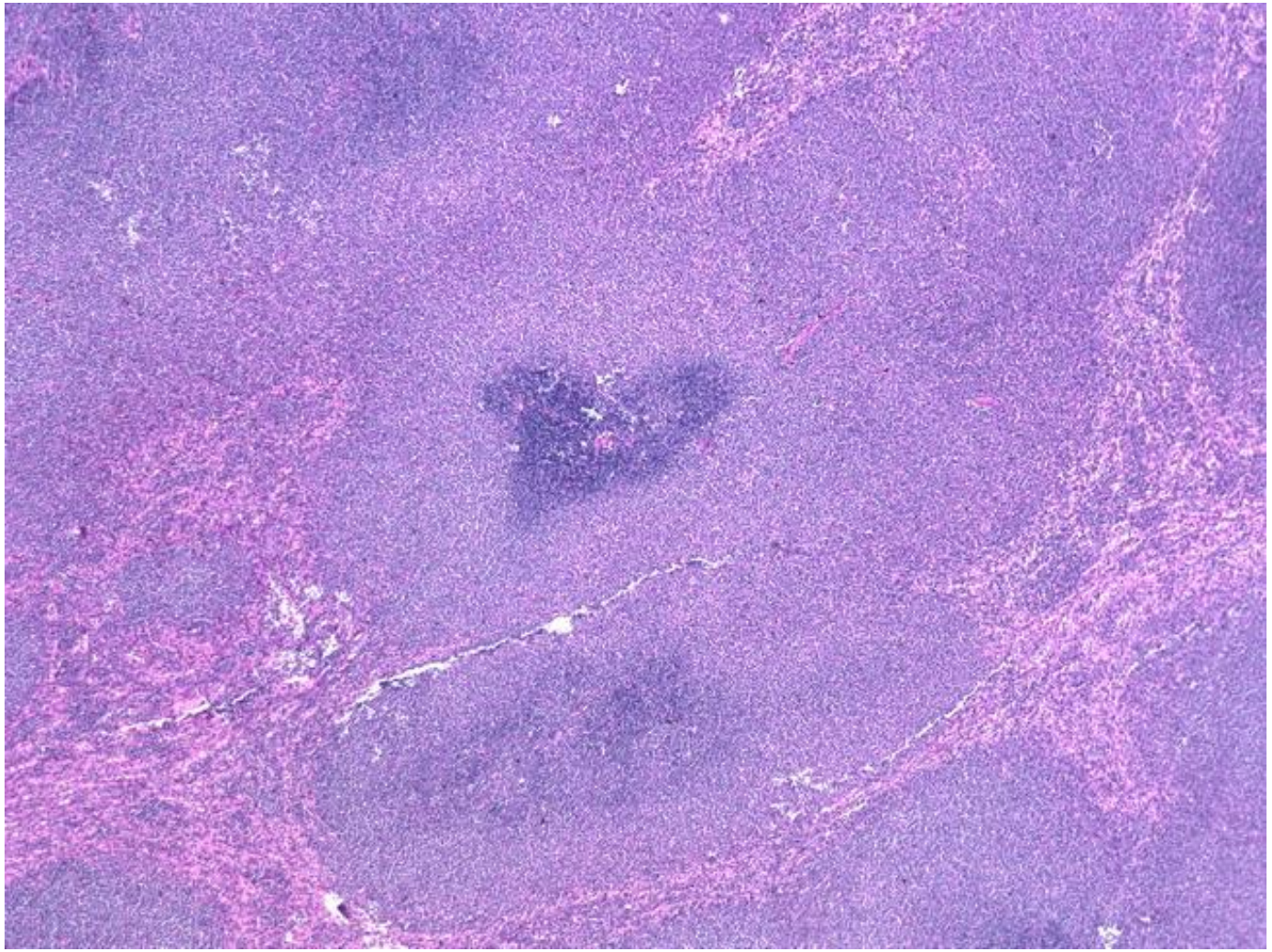


Neoplasia mantellare in situ

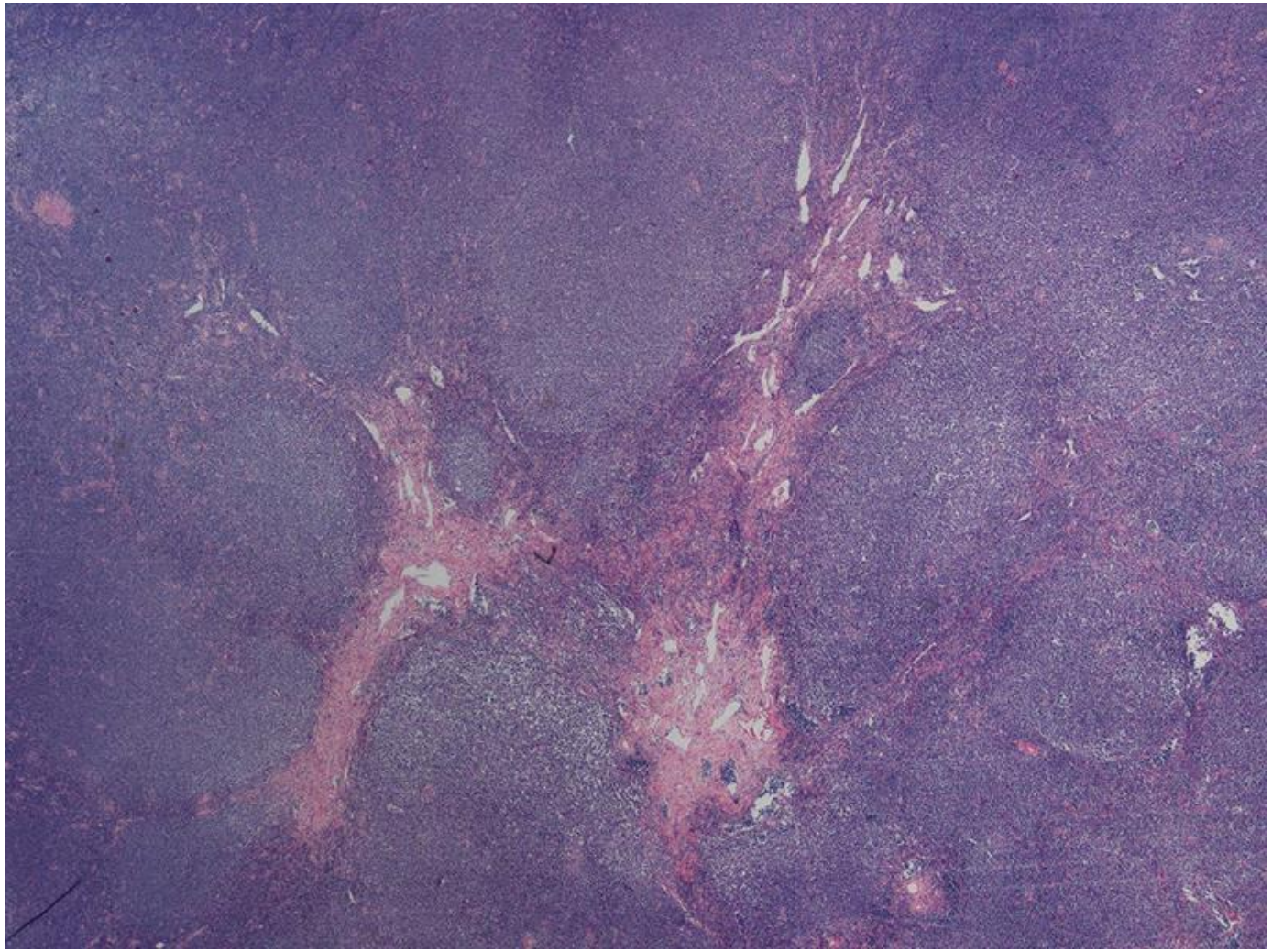


Jaffe et al. Hematopathology 2° ed.

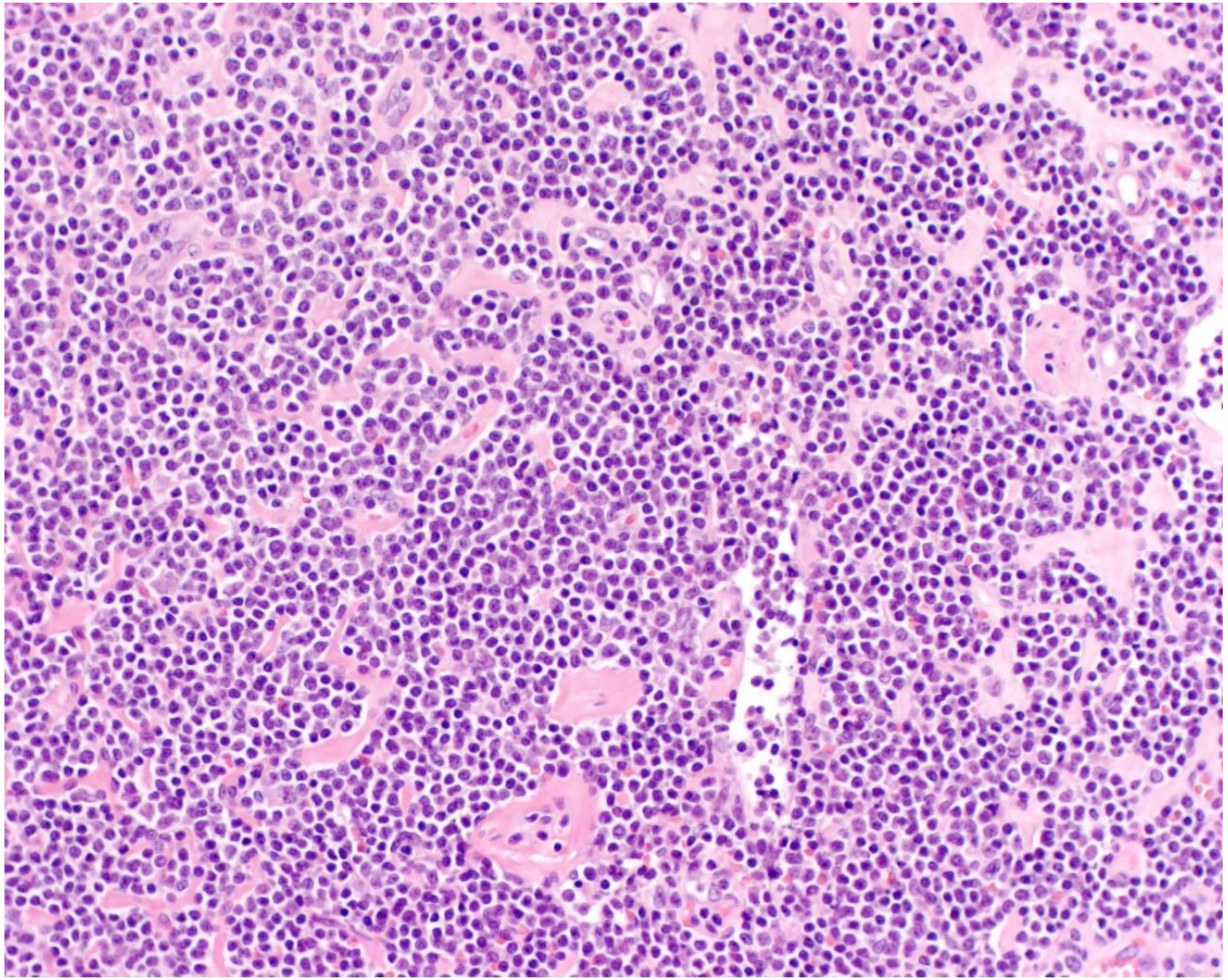
Pattern mantellare



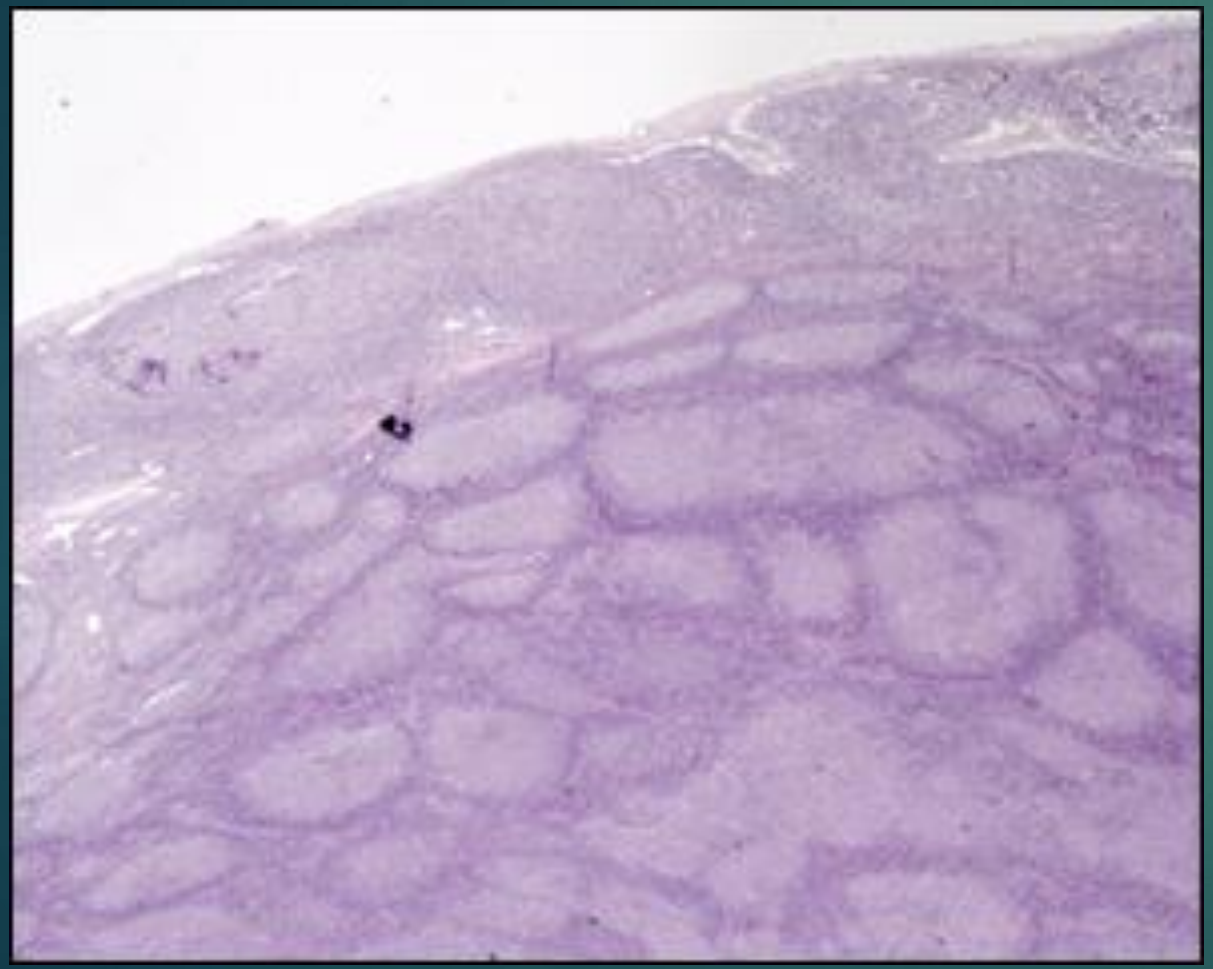
Pattern nodulare

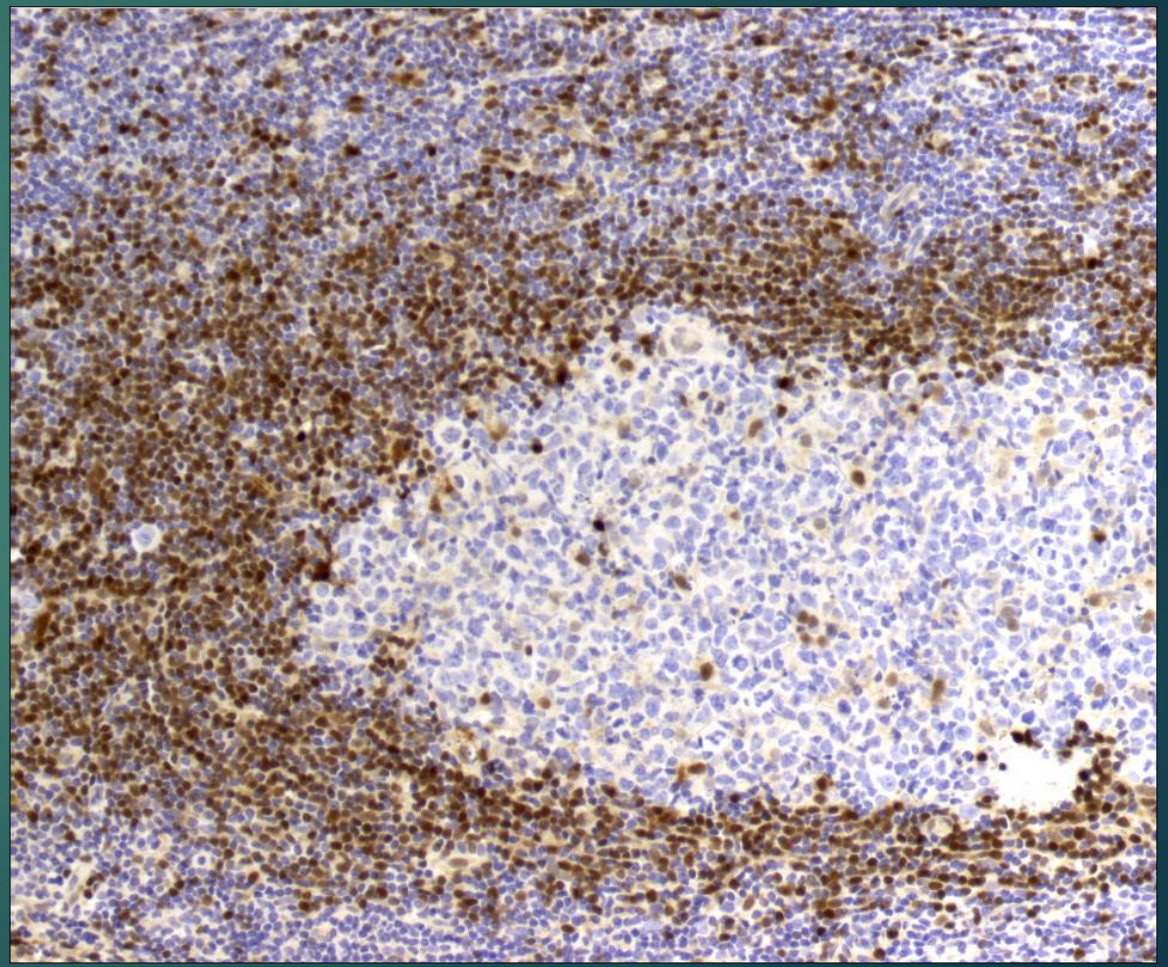


Pattern diffuso



Linfoma composito

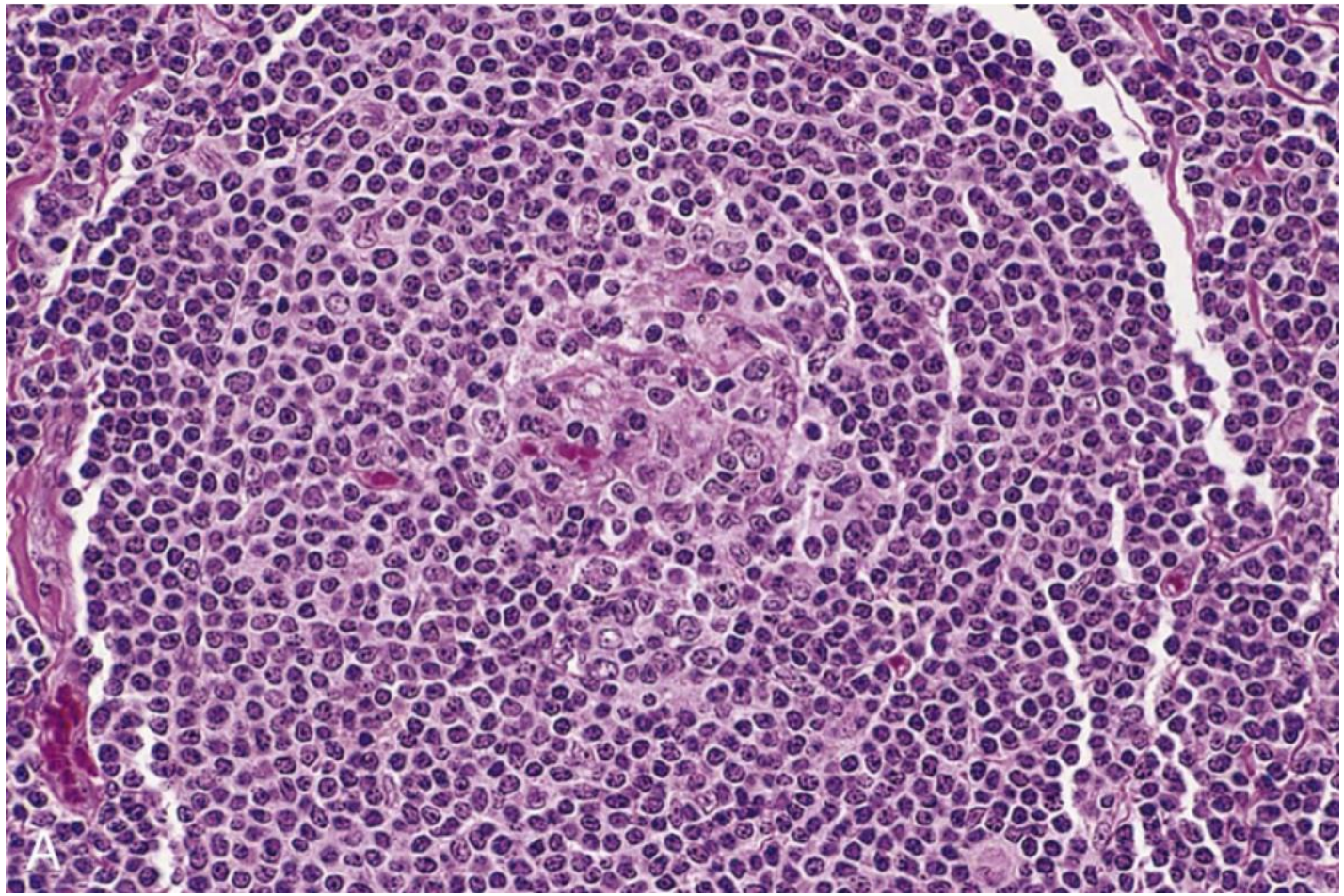




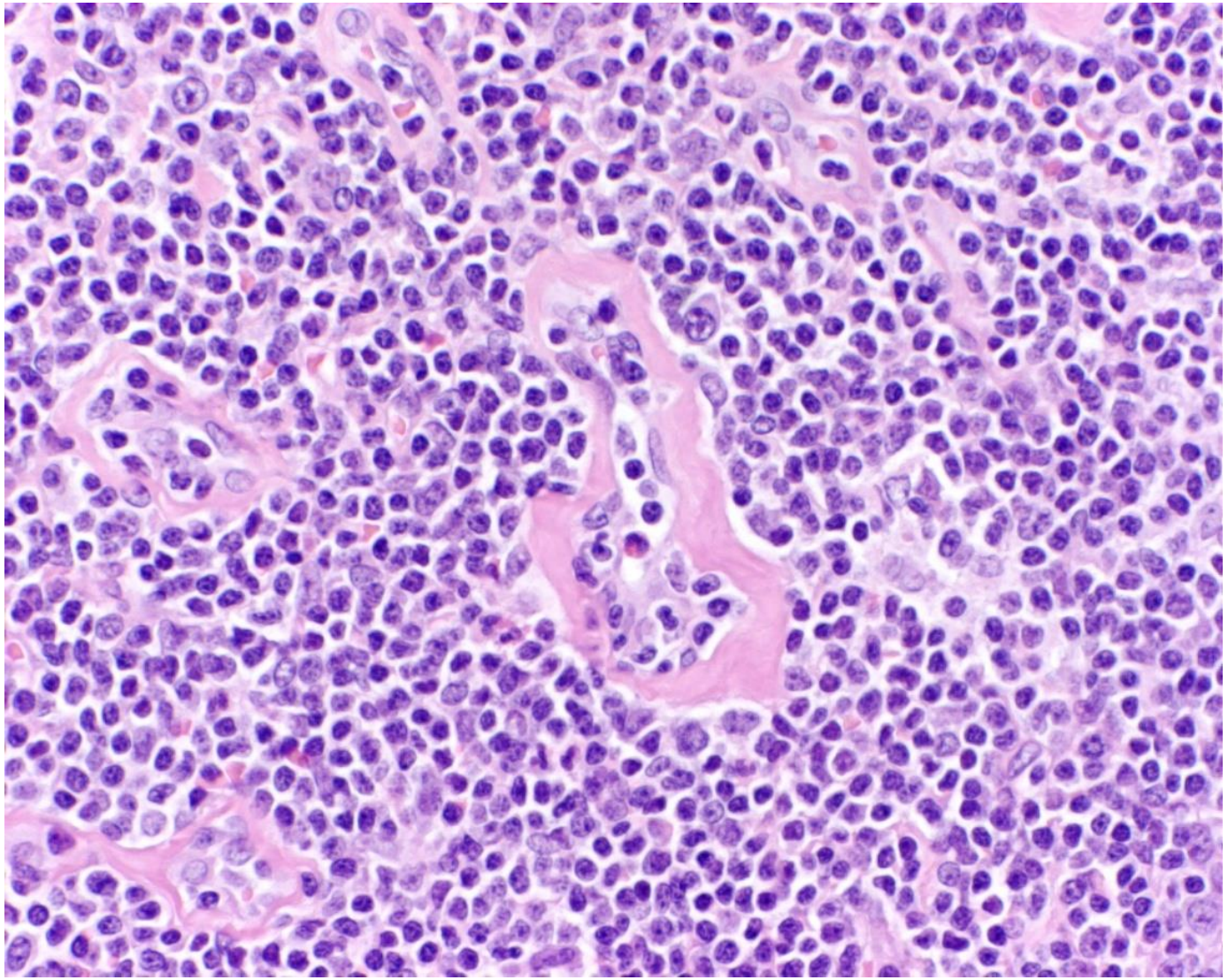
Zamò et al. Virchows Arch 2006

Morfologia classica

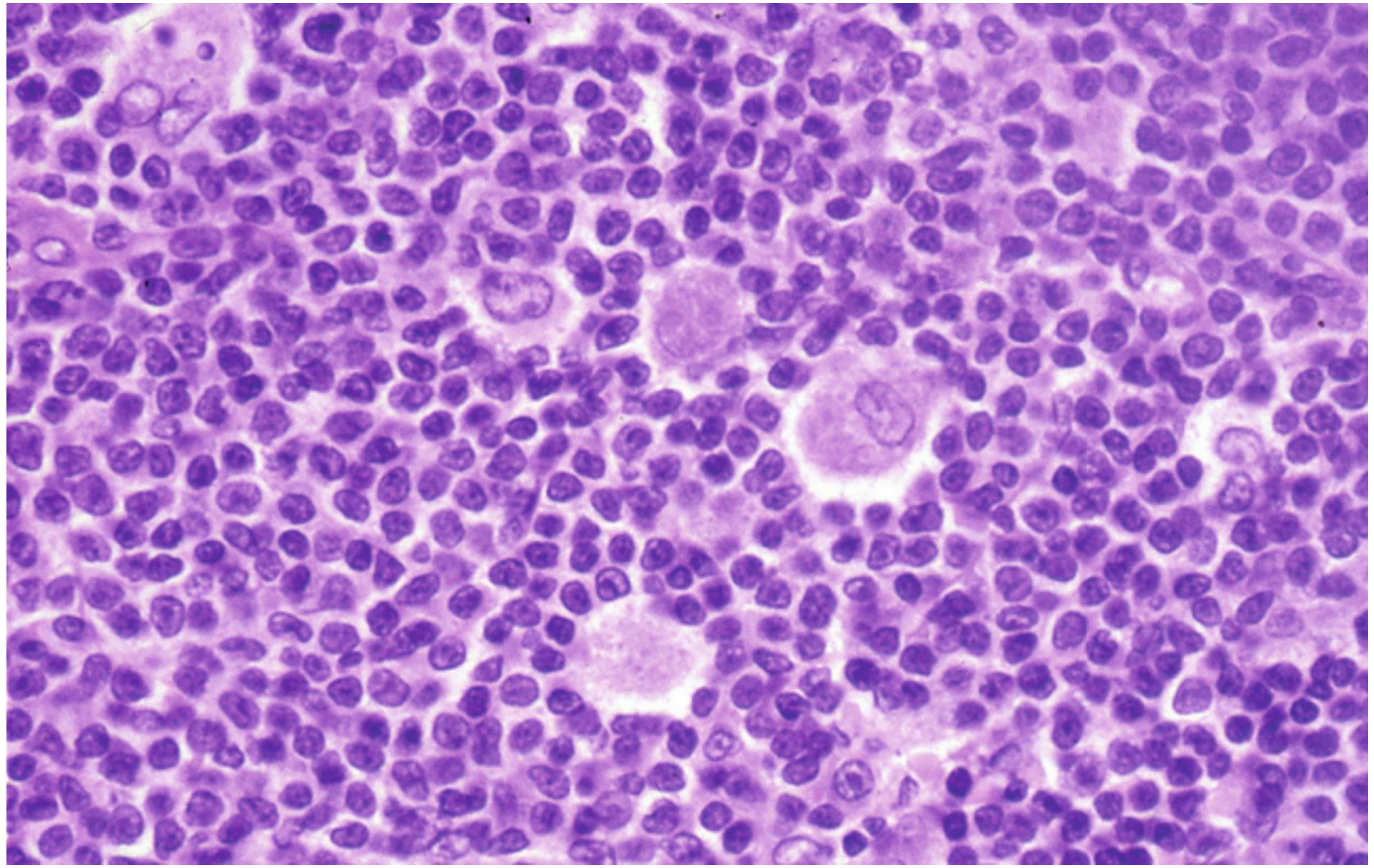
- Proliferazione nodulare o diffusa
- Elementi medio-piccoli, monotoni



Sclero-jalinosi vascolare

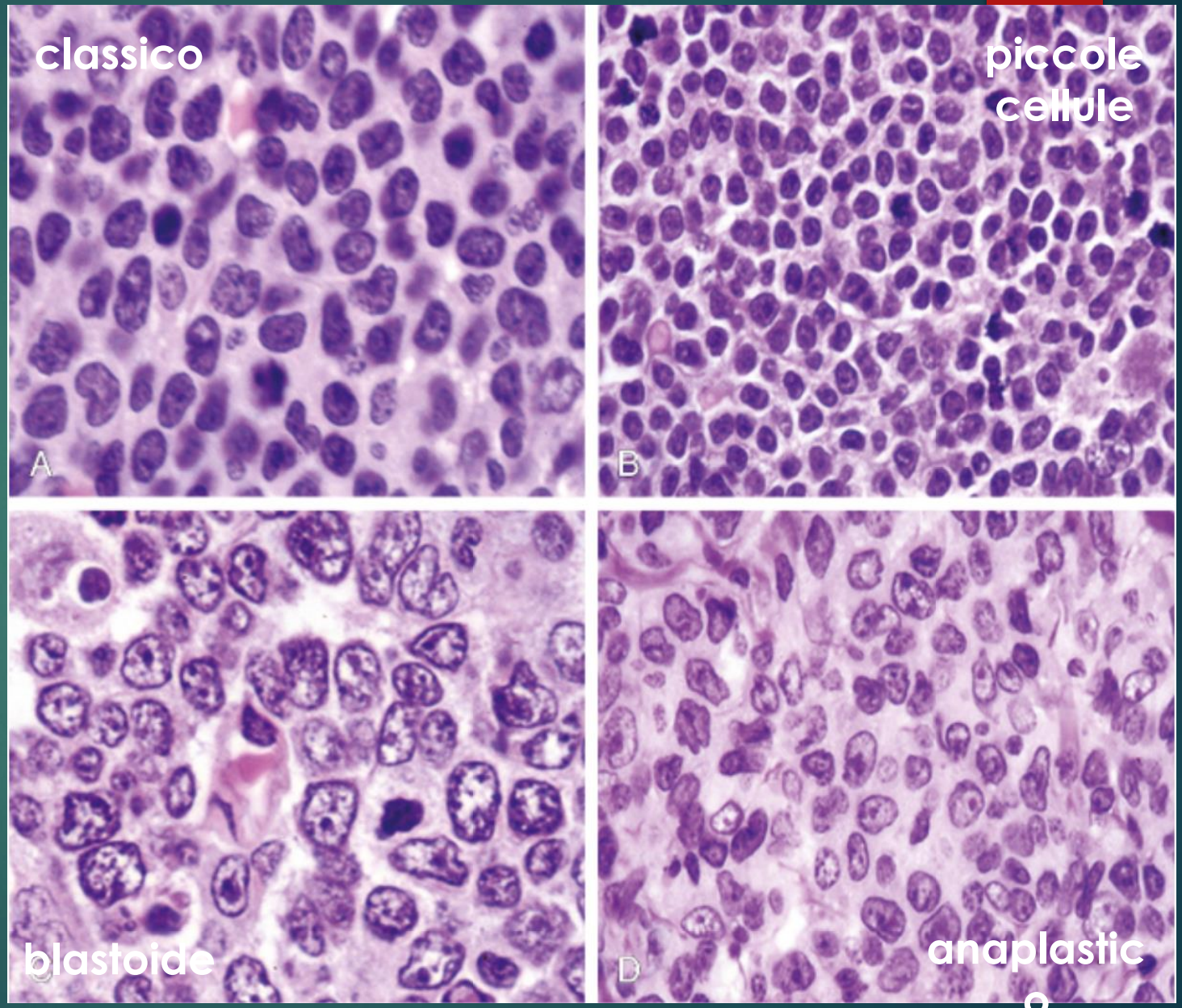


Istiociti rosa



Morfologia citologica

- Classico
- Piccole cellule (tipo CLL)
- Blastoide (tipo LBL)
- Anaplastico (tipo DLBCL)
- (Monocitoide) (tipo MZL)

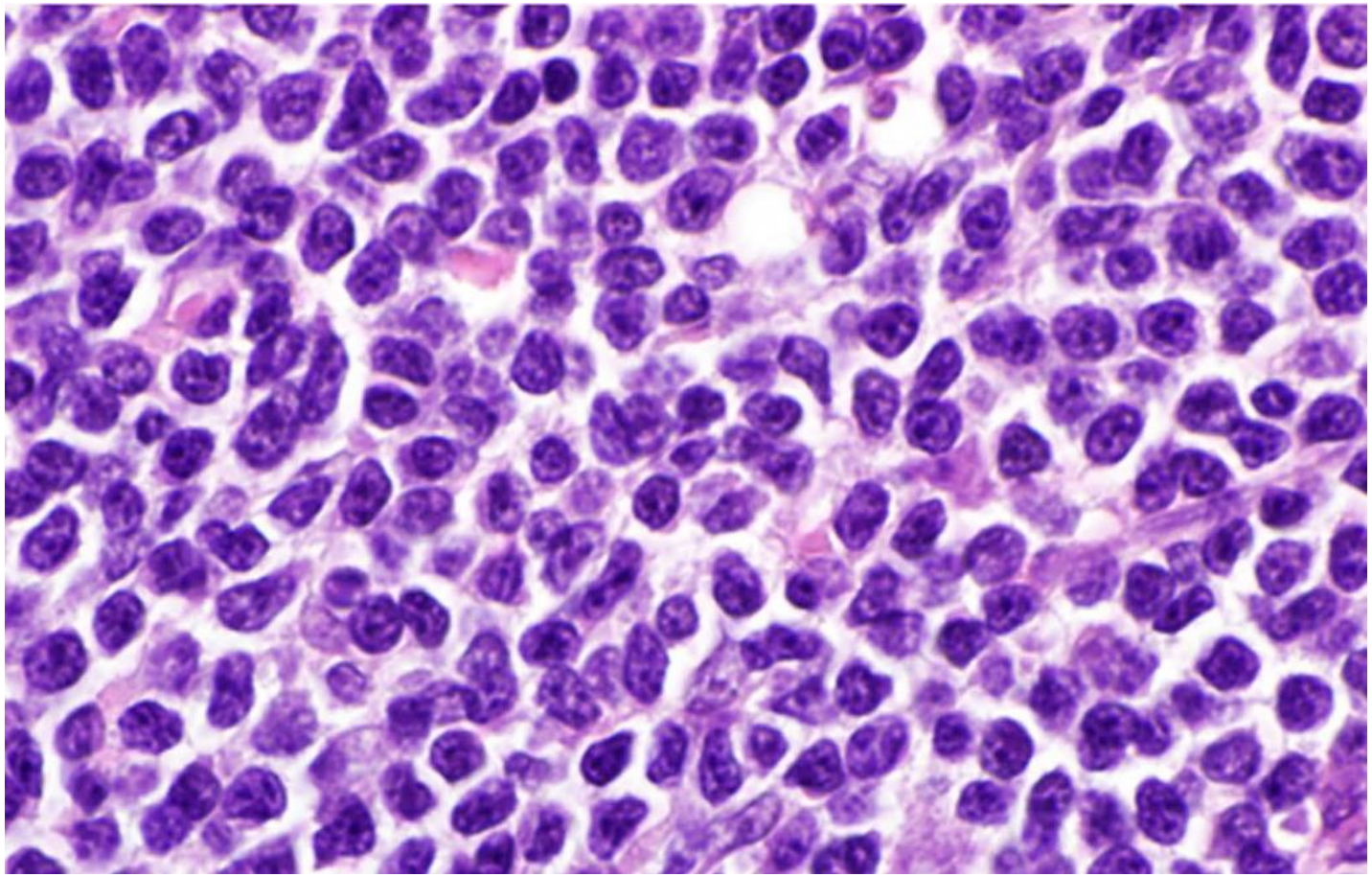


Jaffe et al. Hematopathology 2° ed.

Classico

Dreyling, Klapper, Rule

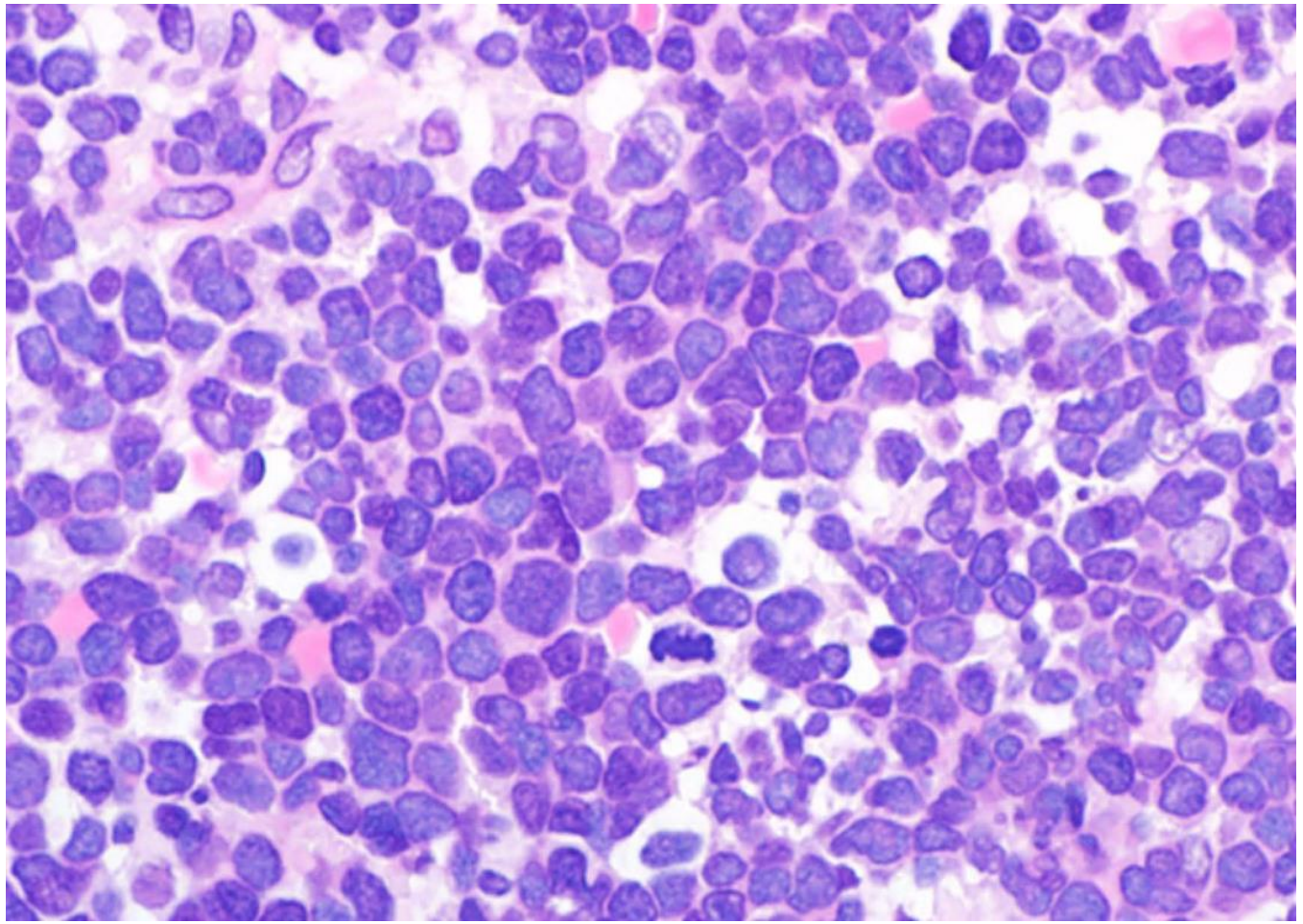
Blood 2018 Nov 1



Blastoide

Dreyling, Klapper, Rule

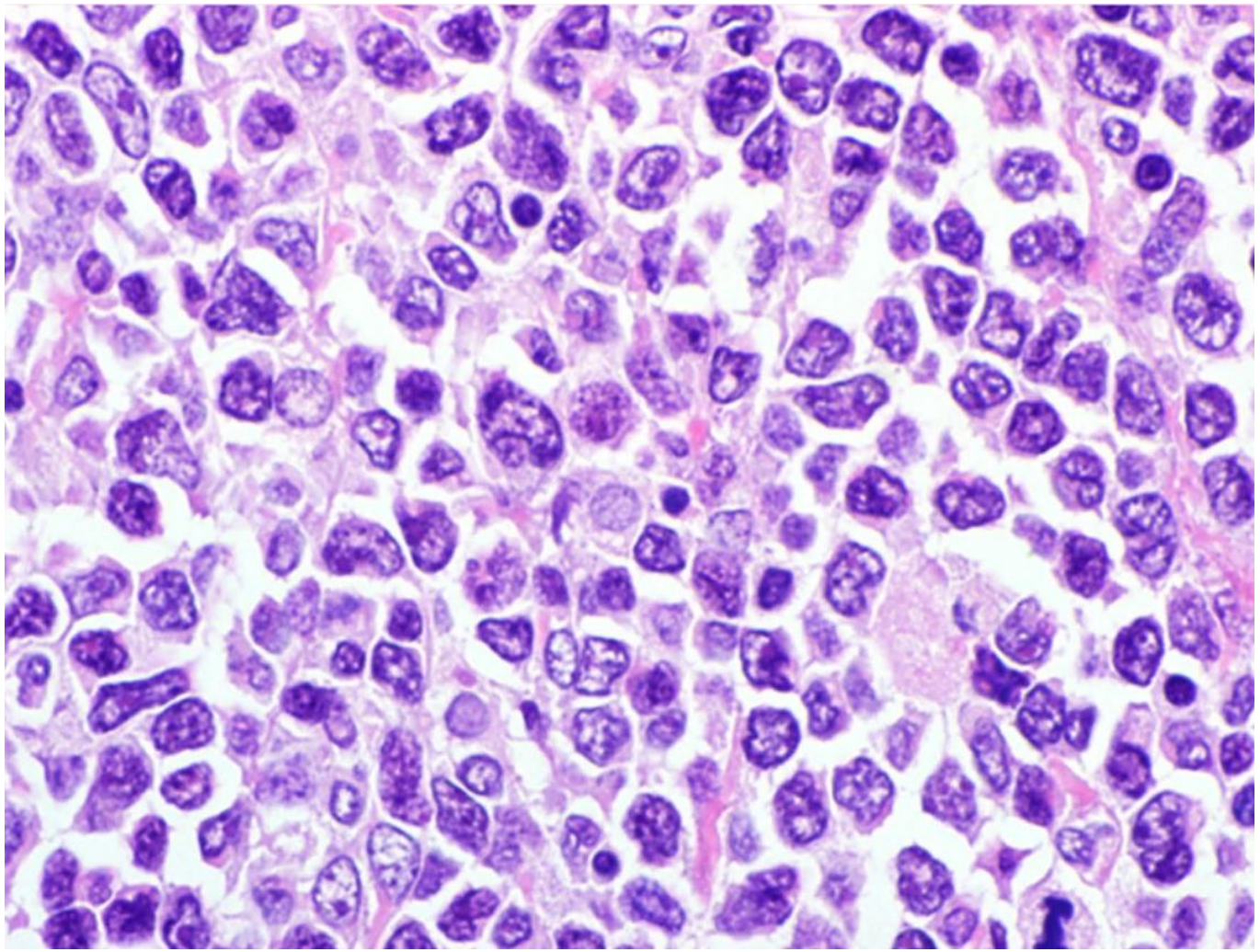
Blood 2018 Nov 1



Pleomorfo

Dreyling, Klapper, Rule

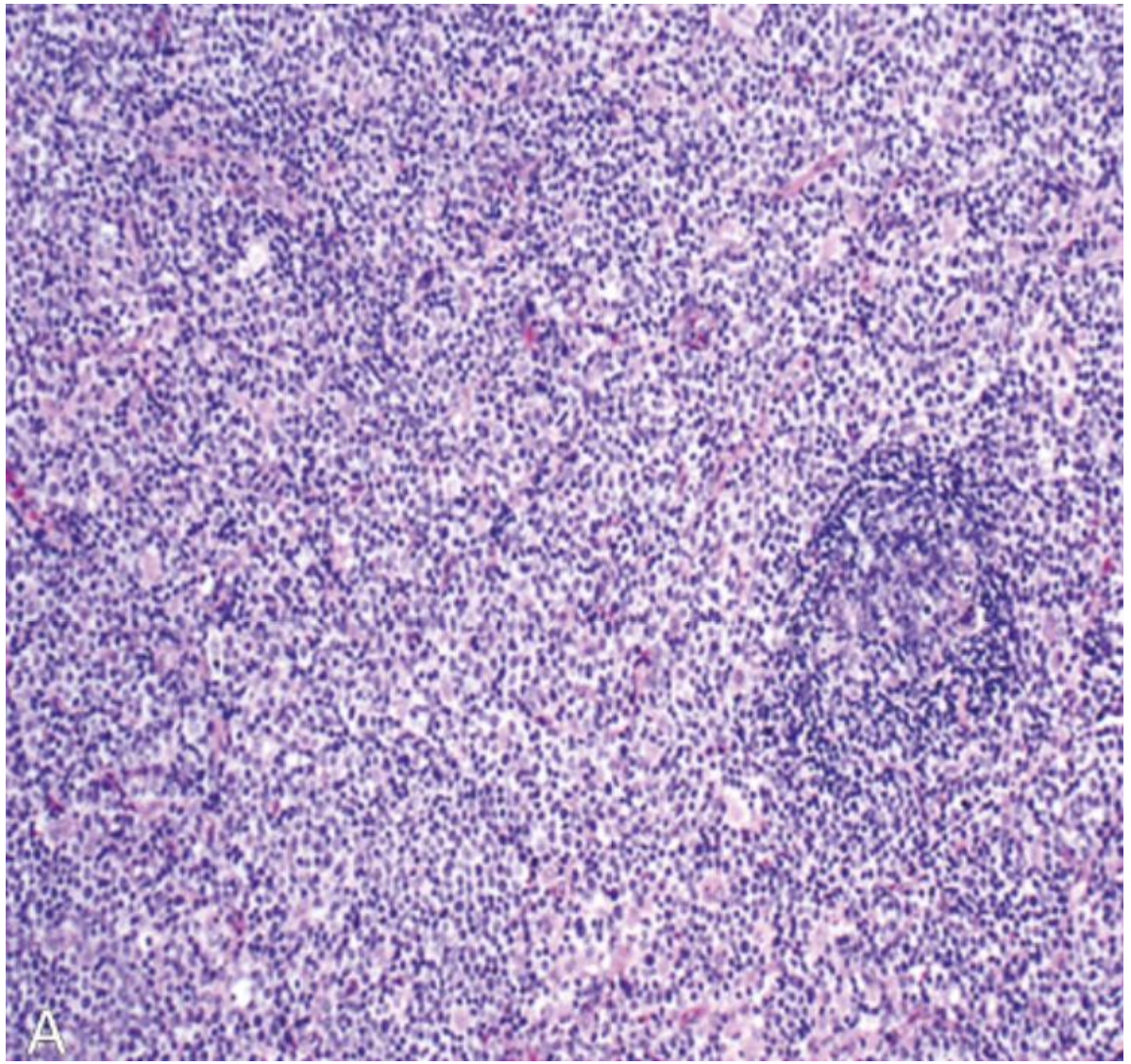
Blood 2018 Nov 1



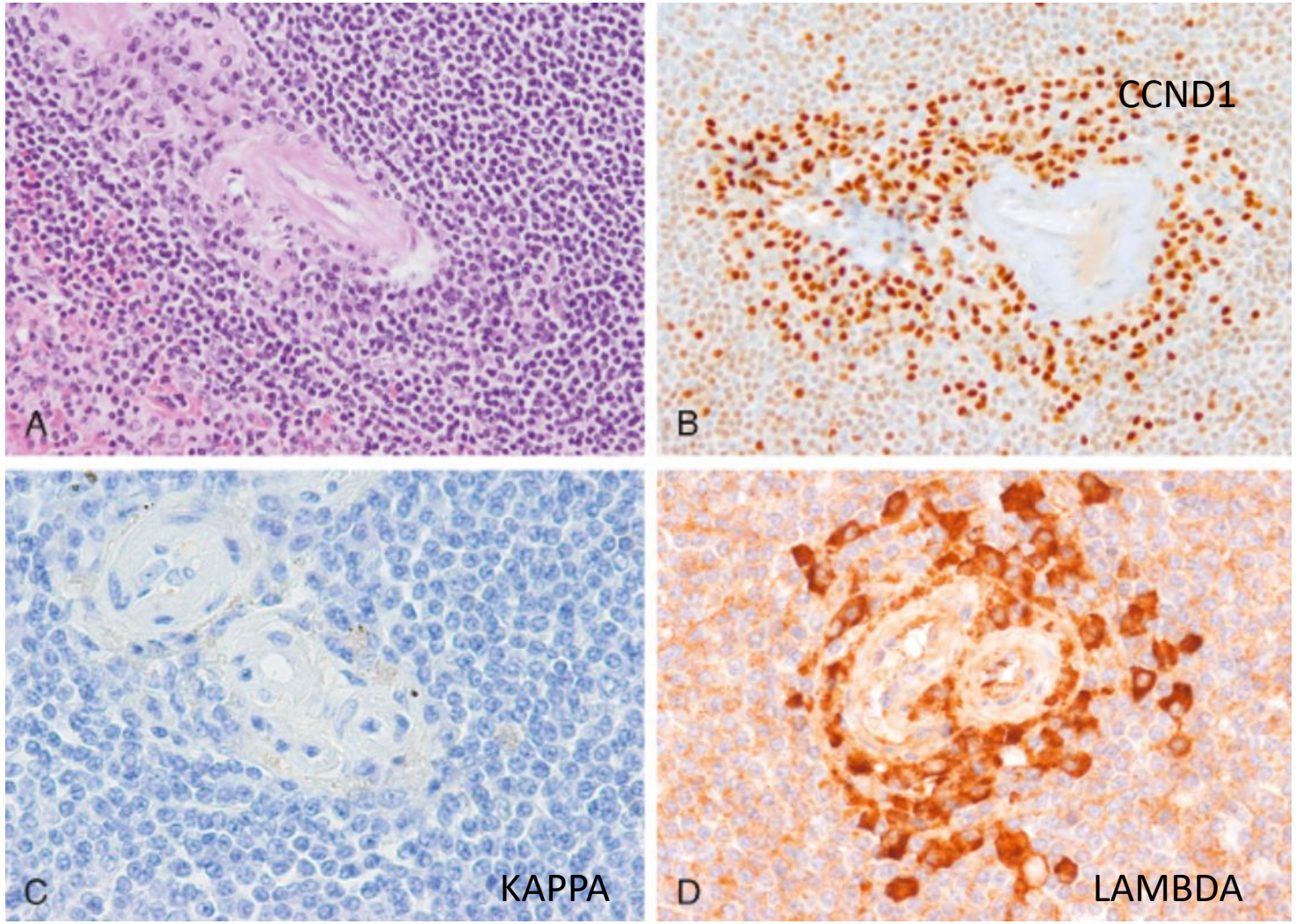
Pattern «marginale»

Jaffe et al.

Hematopathology 2° ed.



Differenziatione plasmacellulare (SOX11-neg.)

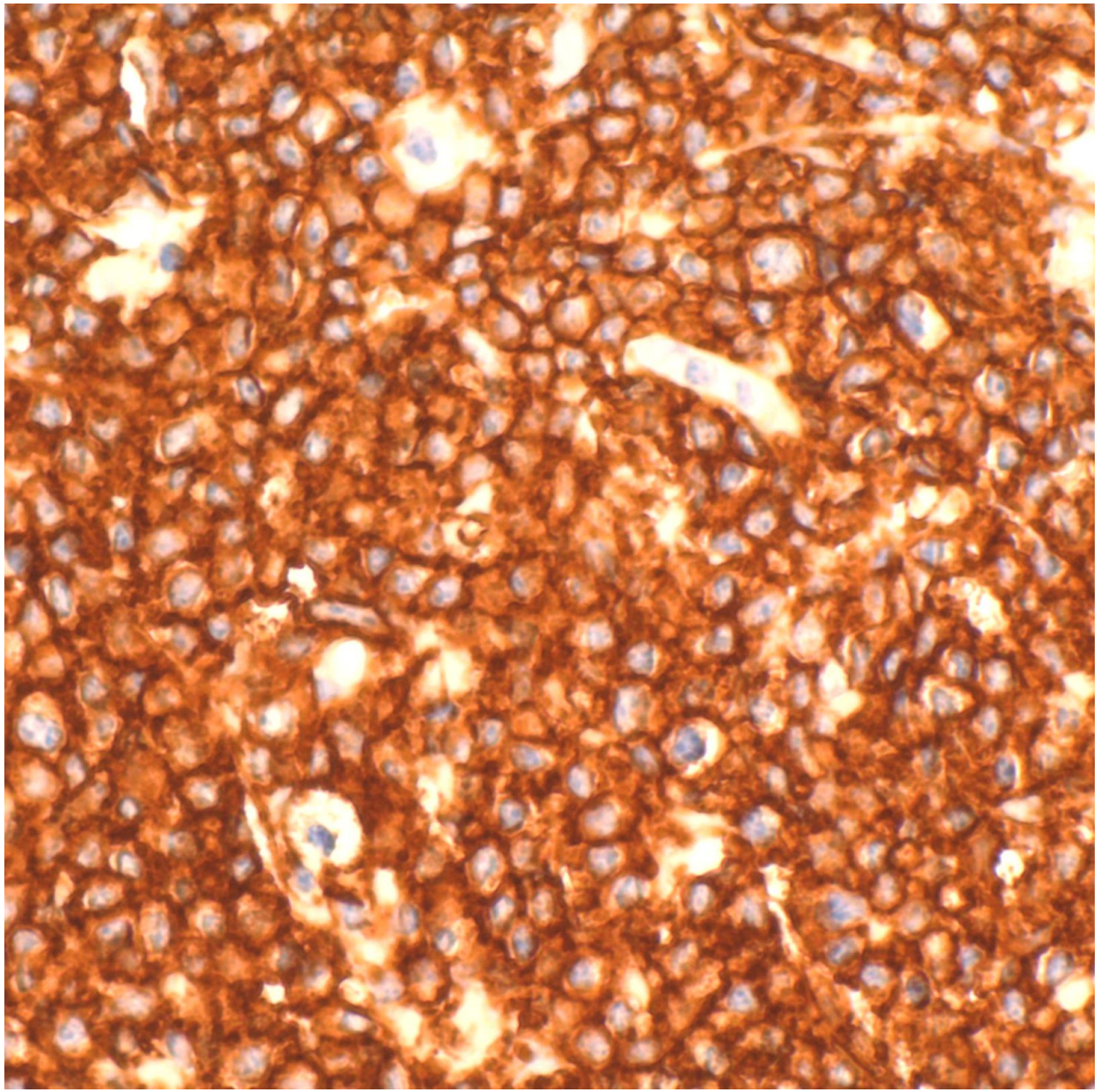


Jaffe et al. Hematopathology 2° ed.

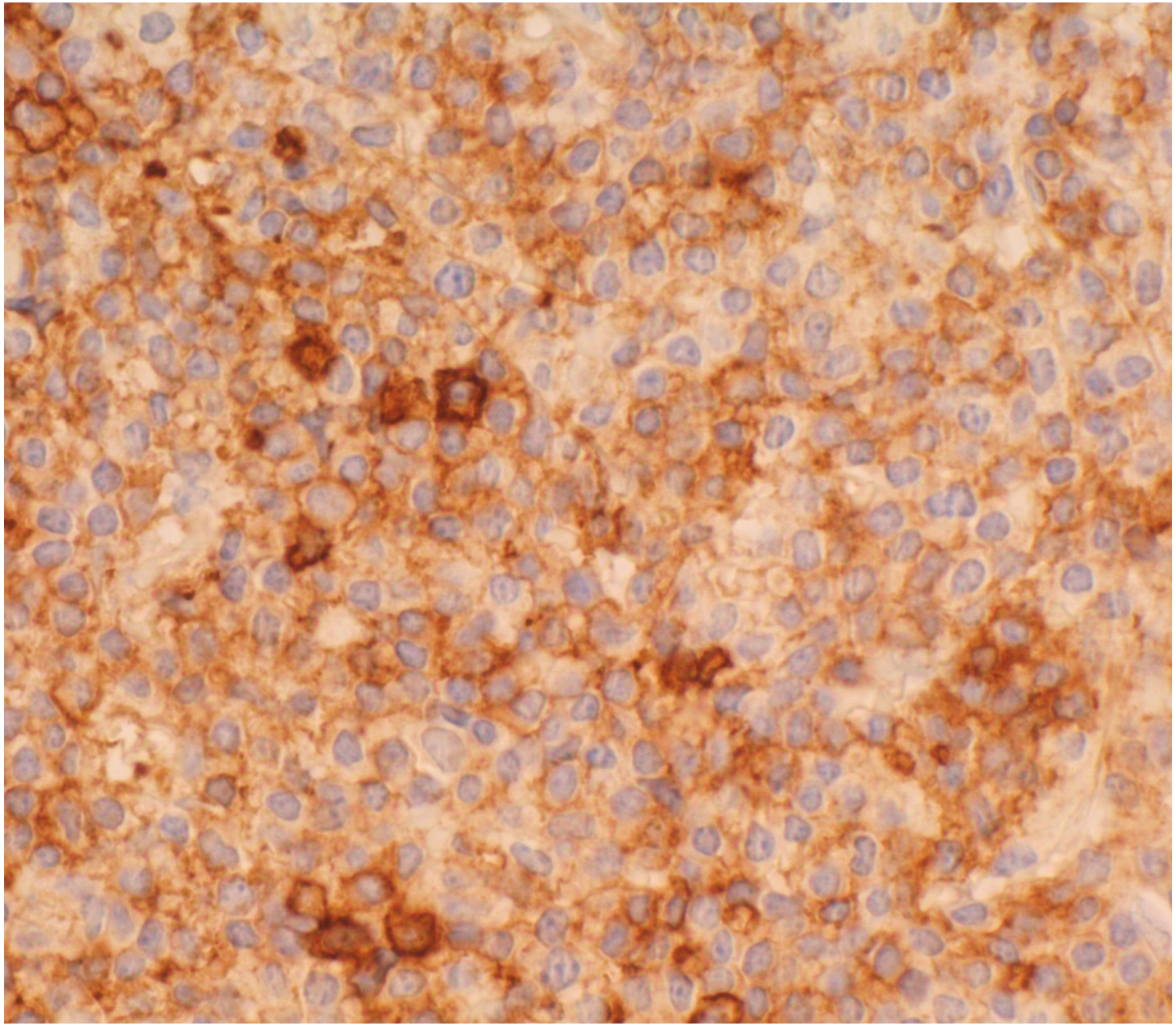
Immunofenotipo

- Marcatori B positivi (alta intensità in citometria a flusso)
- CD5 positivo
- Ciclina D1 positivo (90%)
- SOX11 positivo (marcatore più specifico)
- LEF1-negativo (DD B-CLL)

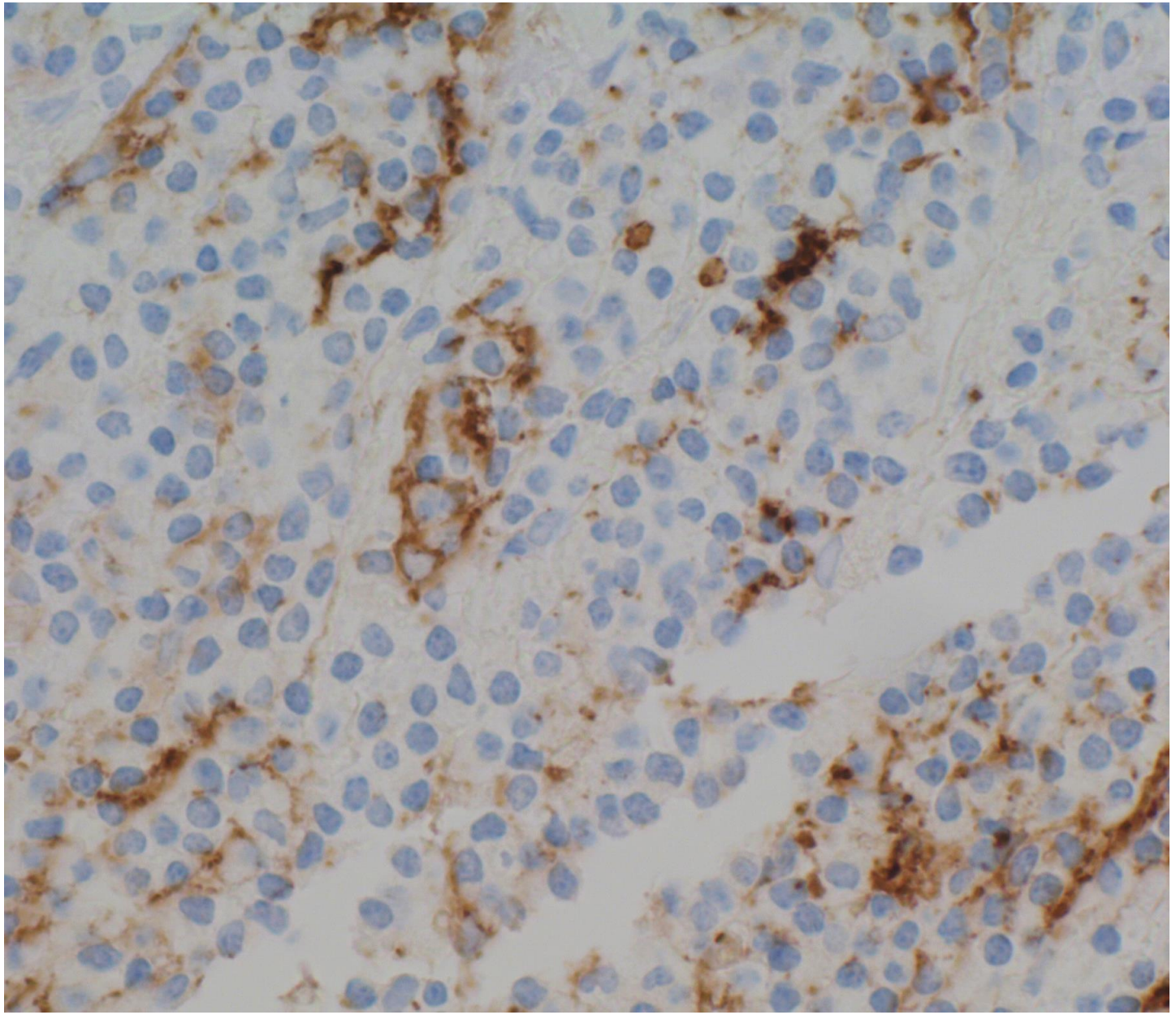
CD20



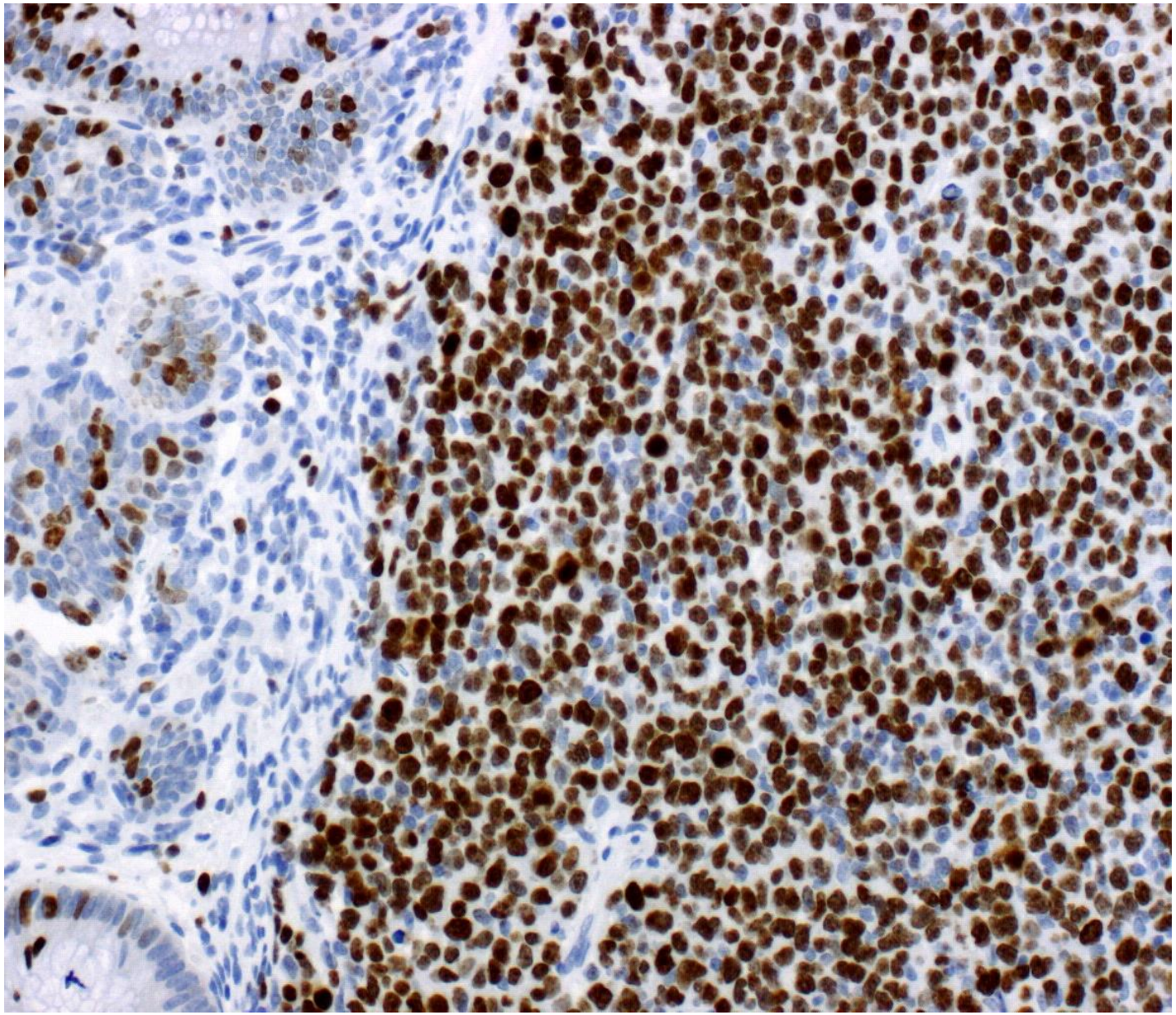
CD5



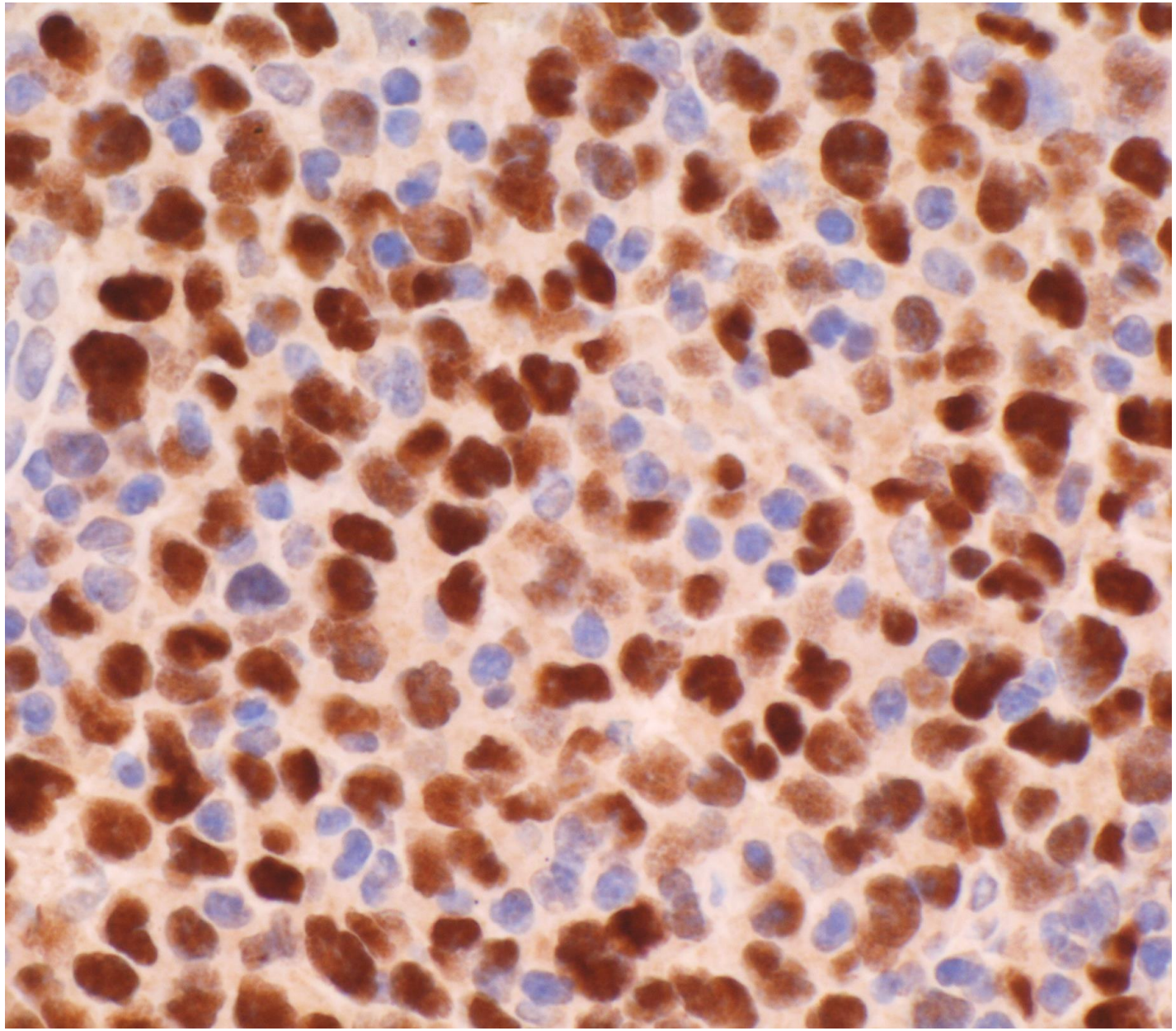
CD23



CCND1



SOX11



Immunofenotipo variante

Espressione di marcatori anomali:

- CD10, BCL6, CD23

Assenza di marcatori tipici:

- Ciclina D1
- SOX11
- CD5

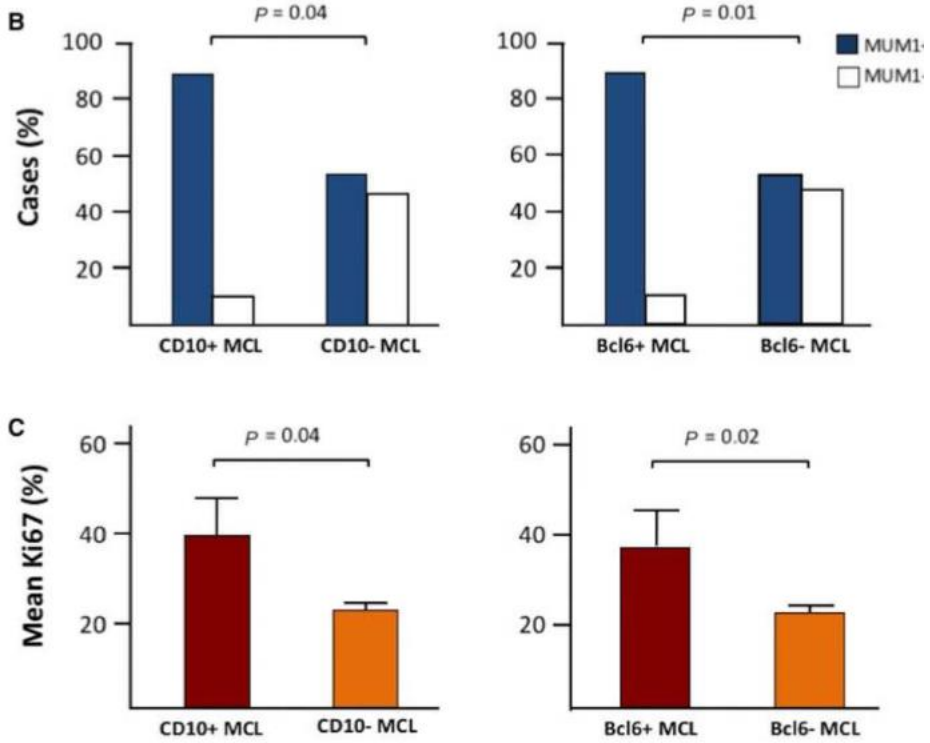
Histopathology

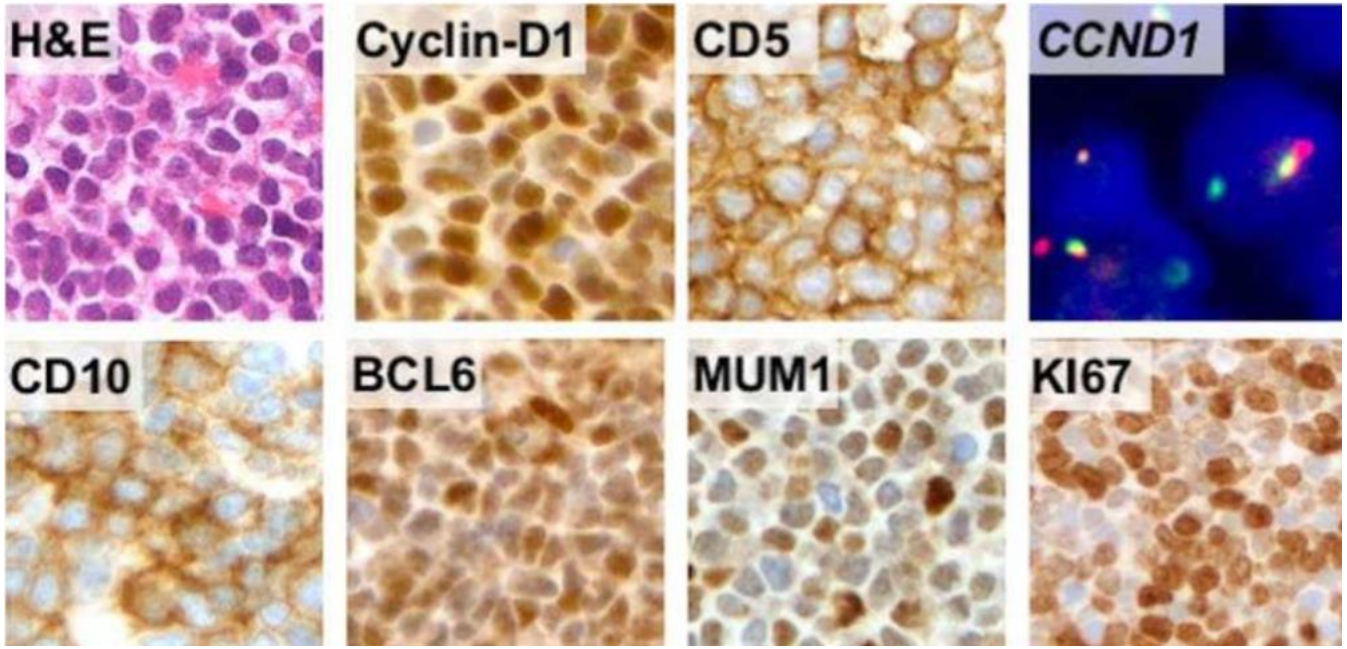
Histopathology 2017, **71**, 769–777. DOI: 10.1111/his.13286

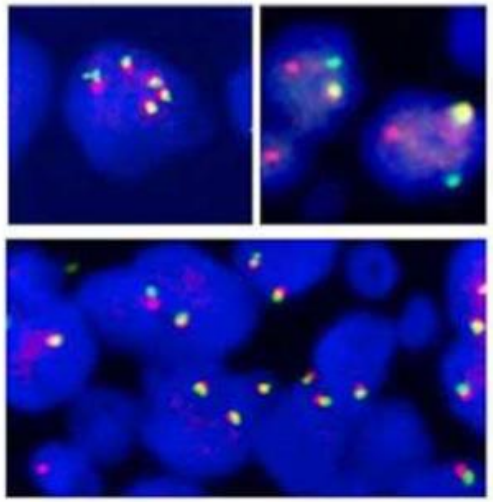
Aberrant expression of CD10 and BCL6 in mantle cell lymphoma

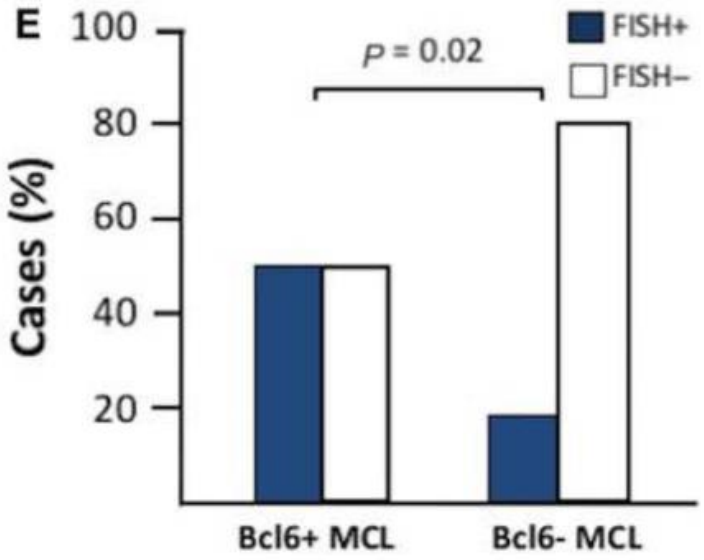
Marco Pizzi,[1] Claudio Agostinelli,[2] Simona Righi,[2] Anna Gazzola,[2] Claudia Mannu,[2] Francesca Galuppini,[1] Matteo Fassan,[1] Andrea Visentin,[3] Francesco Piazza,[3] Gianpietro C Semenzato,[3] Massimo Rugge[1] & Elena Sabattini[2]

[1]*Surgical Pathology and Cytopathology Unit, Department of Medicine-DIMED, University of Padova, Padova,* [2]*Haematopathology Unit, Department of Hematology and Oncology/Department of Experimental Diagnostic and Specialty Medicine, Sant'Orsola University Hospital, Bologna, and* [3]*Hematology and Clinical Immunology Unit, Department of Medicine-DIMED, University of Padova, Padova, Italy*









MCL ciclina D1-negativo

Circa il 5% dei casi classici

Profilo di espressione genica simile ai casi ciclina D1-positivi

Spesso iperespressione di ciclina D2 o D3 (non specifica)

Mcl t(11;14) negativo

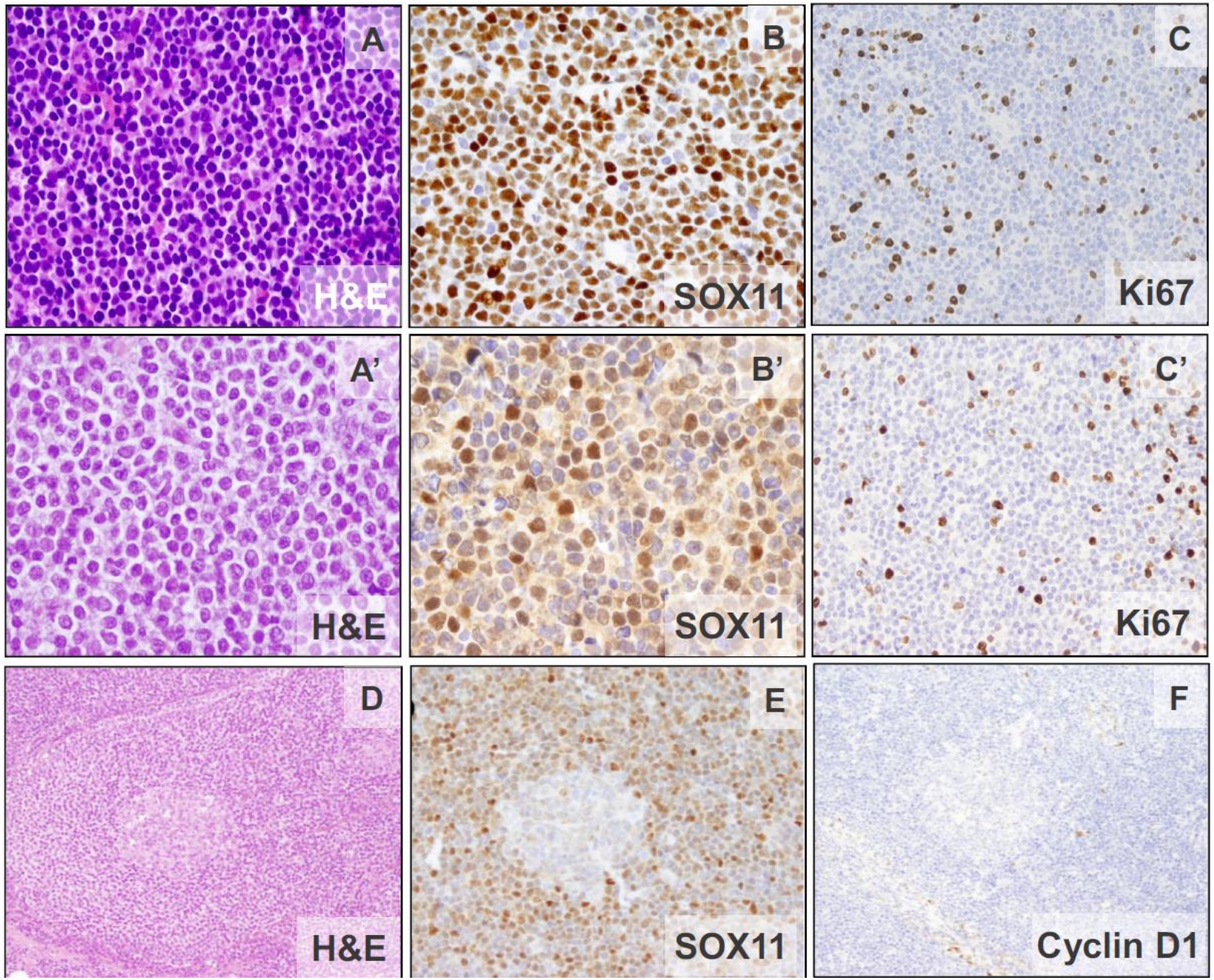
BLOOD, 21 FEBRUARY 2013 • VOLUME 121, NUMBER 8

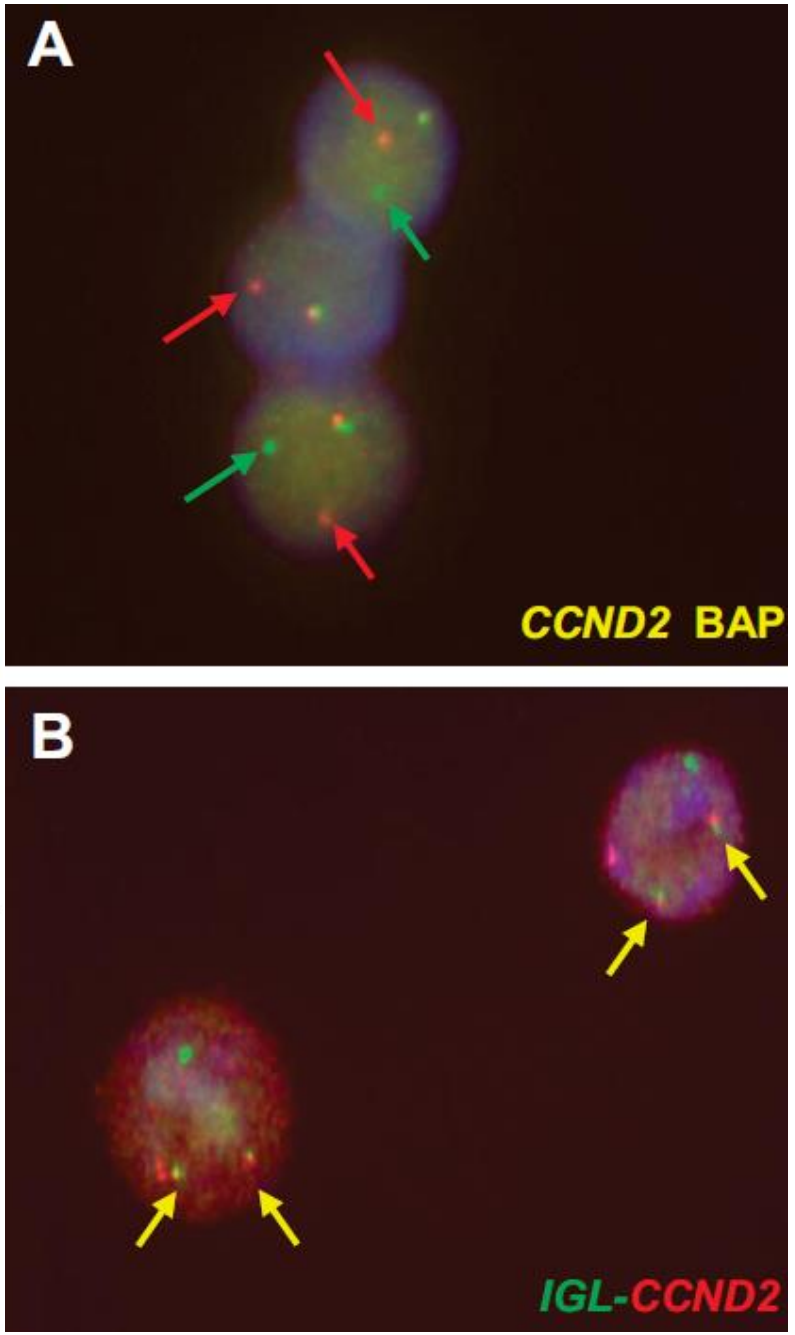
CCND2 rearrangements are the most frequent genetic events in cyclin D1⁻ mantle cell lymphoma

*Itziar Salaverria,[1,2] *Cristina Royo,[1] Alejandra Carvajal-Cuenca,[1] Guillem Clot,[1] Alba Navarro,[1] Alejandra Valera,[1] Joo Y. Song,[3] Renata Woroniecka,[4] Grzegorz Rymkiewicz,[5] Wolfram Klapper,[6] Elena M. Hartmann,[7] Pierre Sujobert,[8] Iwona Wlodarska,[9] Judith A. Ferry,[10] Philippe Gaulard,[8] German Ott,[11] Andreas Rosenwald,[7] Armando Lopez-Guillermo,[12] Leticia Quintanilla-Martinez,[13] Nancy L. Harris,[10] Elaine S. Jaffe,[3] Reiner Siebert,[2] Elias Campo,[1] and Sílvia Beà[1]

Table 1. Genetic, morphologic, and immunophenotypical parameters of 40 cyclin D1⁻/SOX11⁺ MCL patients

Parameter	n	%
***CCND2* translocation**		
IGH-CCND2	3/40	8
IGK-CCND2	10/40	25
IGL-CCND2	5/40	13
CCND2-break*	2/40	5
CCND2-?†	2/40	5
Negative	18/40	45


A
H&E
B
SOX11
C
Ki67
A'
H&E
B'
SOX11
C'
Ki67
D
H&E
E
SOX11
F
Cyclin D1


A
CCND2 BAP
B
IGL-CCND2

FISH

La t(11;14) è rilevabile con sonde commerciali

Solitamente non eseguita se il caso è tipico (CCND1+)

Traslocazioni varianti

t(2;12)(p12;p13) IGK@-CCND2

t(12;22)(p13;q22) IGL-CCND2 fusion

Cryptic t(12;14)(p13;q32)/IGH-CCND2

CCND2 breaks with unidentified partner

Cryptic cyclin D3 rearrangements

MCL SOX11-negativo

Circa 10%

Può dipendere da clone anticorpale e interpretazione

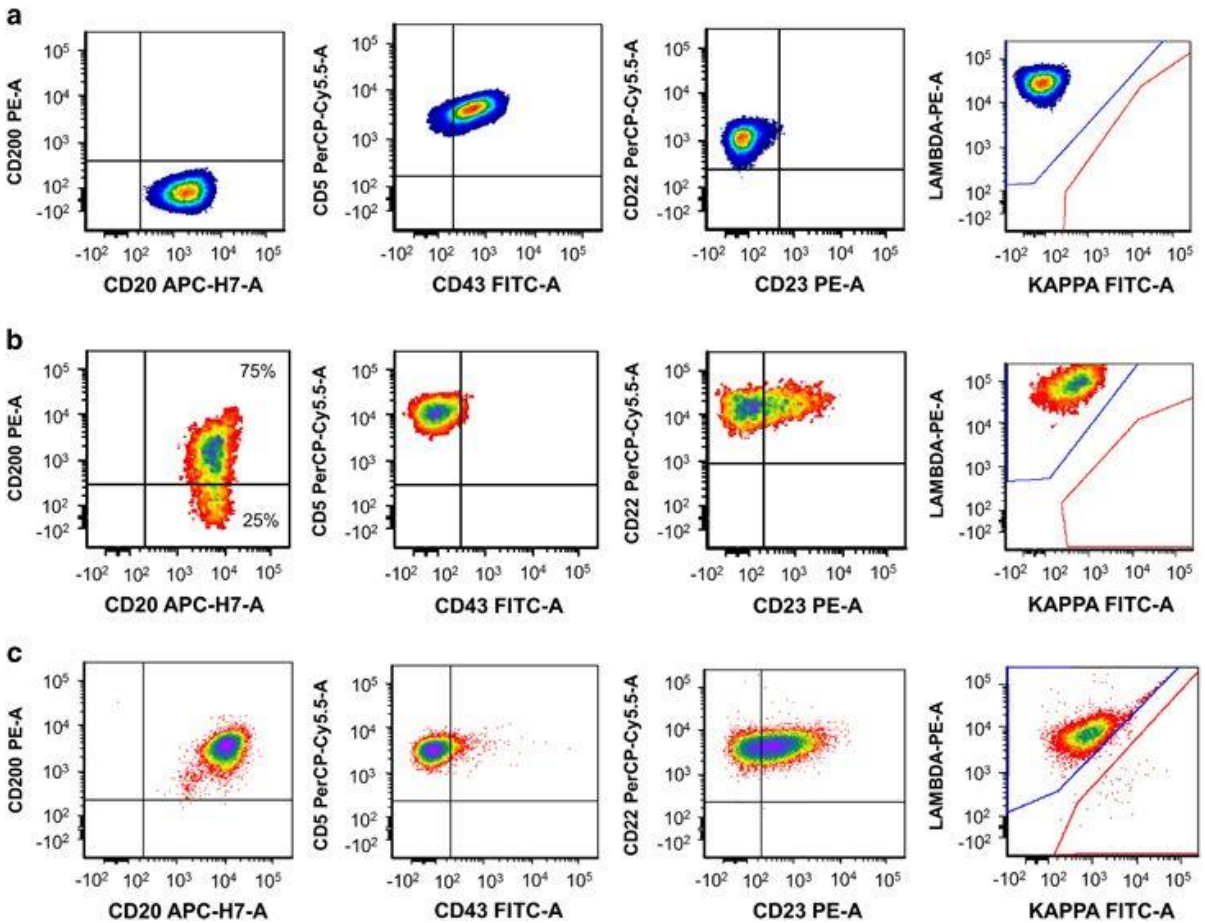
Soglie di positività non definite

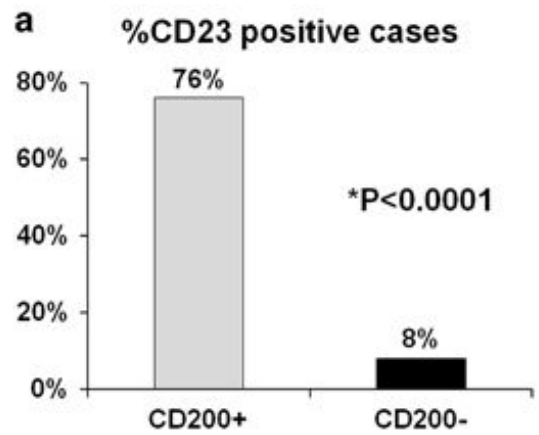
MCL SOX11-negativo

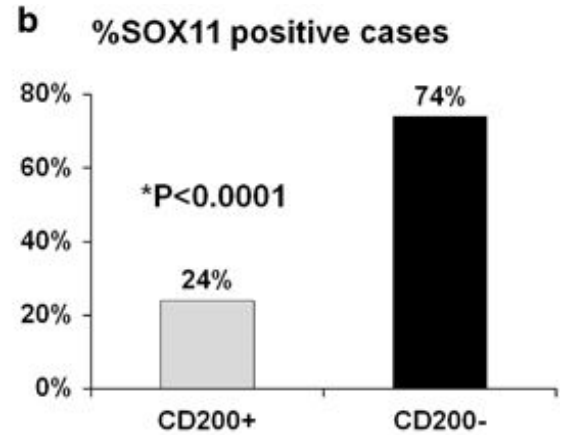
Correlazione con espressione di CD200 e CD23, basso CD5

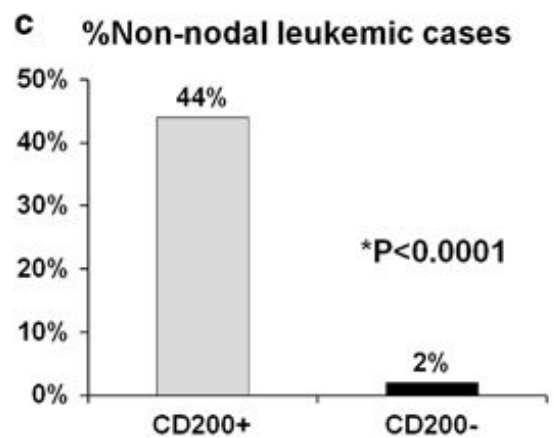
Spesso variante a piccole cellule

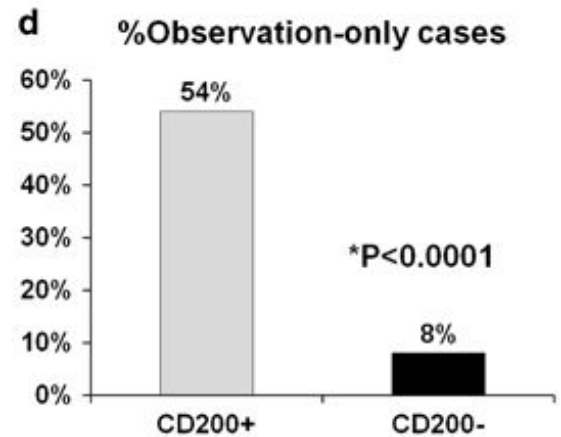
Correlazione con forma indolente non-nodale











Hu Modern Pathology 2018

SOX11

Hodgkin lymphoma	0/10 (0)
Mantle cell lymphoma	24/28 (86)
Follicular lymphoma	1/58 (2)
Burkitt lymphoma	3/16 (13)
Large B cell lymphoma	0/110 (0)
T/B cell lymphoblastoma	3/22 (14)
MALT	0/43 (0)
Angioimmunoblastic T cell lymphoma	0/11 (0)
NK/T cell lymphoma	0/5 (0)
Small lymphocytic lymphoma	0/9 (0)
Peripheral T cell lymphoma	0/5 (0)

Xu et al. Histopathology 2018

Table 4. SOX11 expression in selected tumours

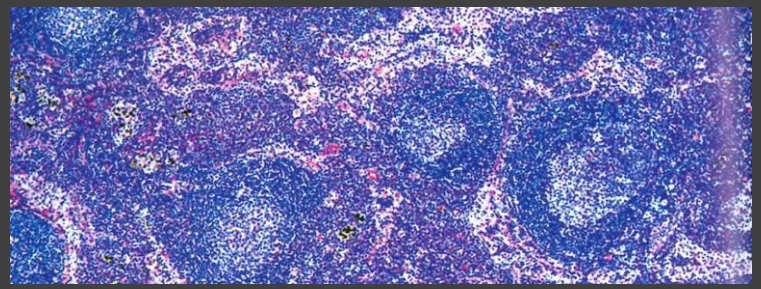
Tumour type	Positive/total (%)				
	Total	3+	2+	1+	–
PNET/EWS	38/38 (100)	15 (39)	17 (45)	6 (16)	0 (0)
Central neurocytoma	9/9 (100)	5 (55)	4 (45)	0 (0)	0 (0)
Lung small cell carcinoma	71/104 (68)	28 (27)	26 (26)	17 (16)	33 (32)
Myxoid liposarcomas	9/9 (100)	5 (56)	4 (44)	0 (0)	0 (0)
Salivary ductal carcinomas	22/24 (92)	13 (54)	8 (33)	1 (4)	2 (8)
Rhabdomyosarcoma	45/50 (90)				
Alveolar rhabdomyosarcoma	17/17 (100)	14 (82)	3 (18)	0 (0)	0 (0)
Embryonal rhabdomyosarcoma	22/23 (96)	11 (48)	12 (52)	0 (0)	1 (0)
Spindle cell rhabdomyosarcoma	4/5 (80)	0 (0)	2 (40)	2 (40)	1 (20)
Pleomorphic rhabdomyosarcoma	1/5 (20)	0 (0)	0 (0)	1 (20)	4 (80)

PNET/EWS, Primitive neuroectodermal tumour/Ewing's sarcoma.

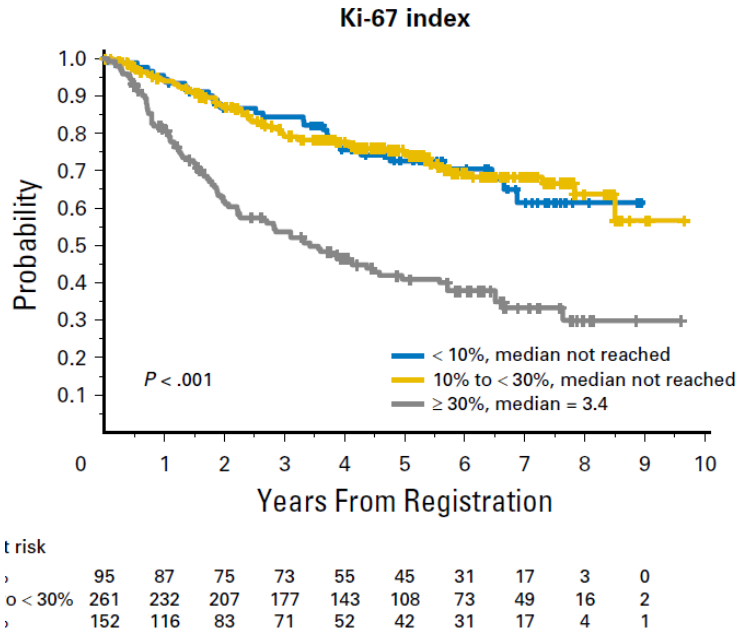
Xu et al. Histopathology 2018

Fattori prognostici patologici

Varianti morfologiche



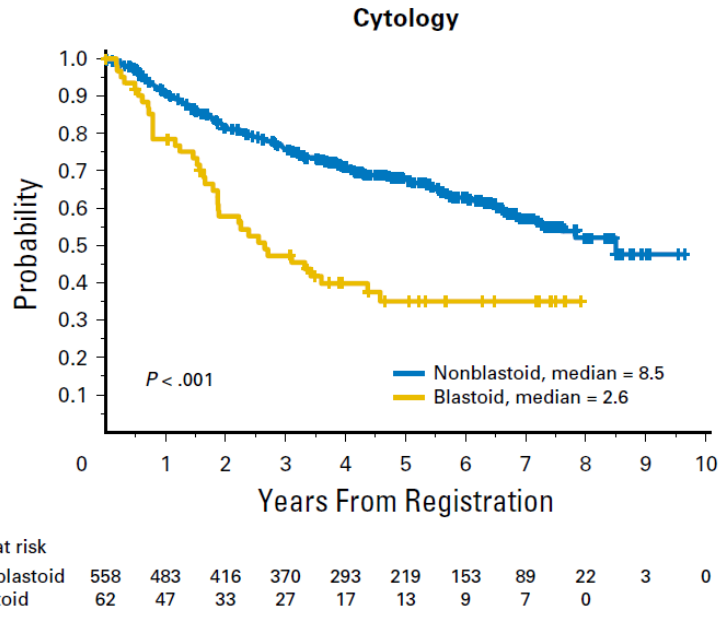
- Blastoide (prognosi peggiore, forse non indipendente)
- A piccole cellule (migliore, correlata a variante leucemica non-nodale)
- Pattern mantellare (migliore)



t risk

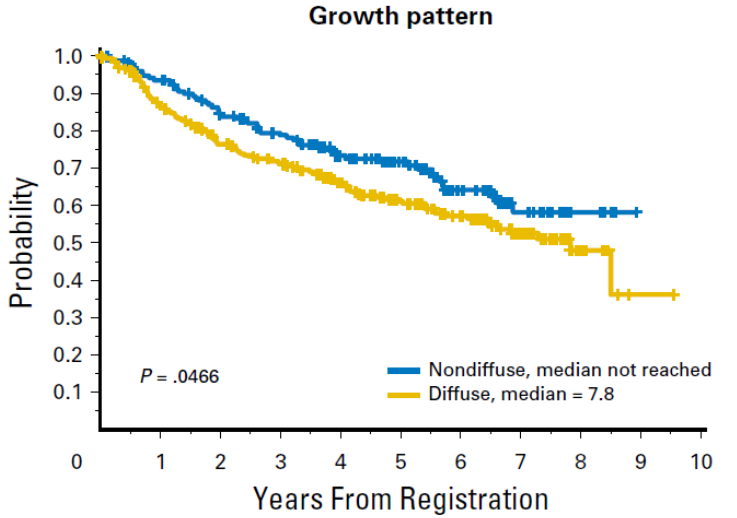
	95	87	75	73	55	45	31	17	3	0
o < 30%	261	232	207	177	143	108	73	49	16	2
	152	116	83	71	52	42	31	17	4	1

B

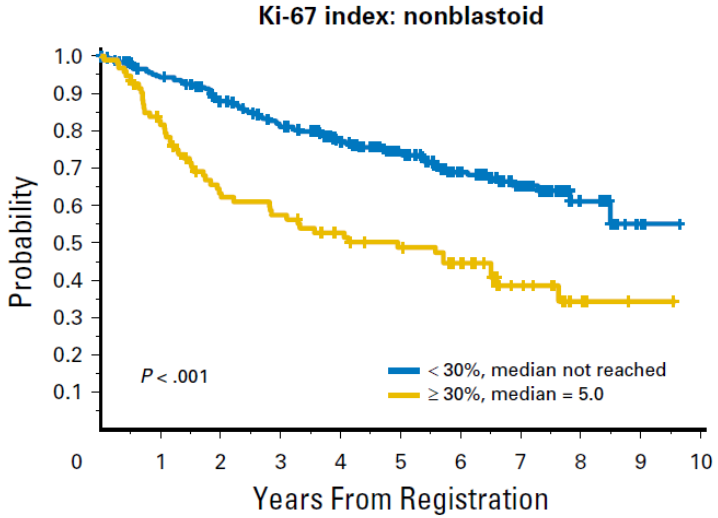


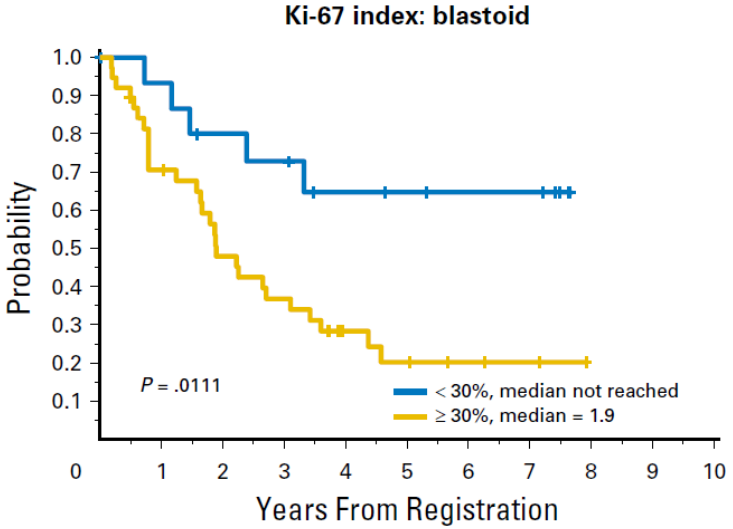
No. at risk

Nonblastoid	558	483	416	370	293	219	153	89	22	3	0
Blastoid	62	47	33	27	17	13	9	7	0		



D

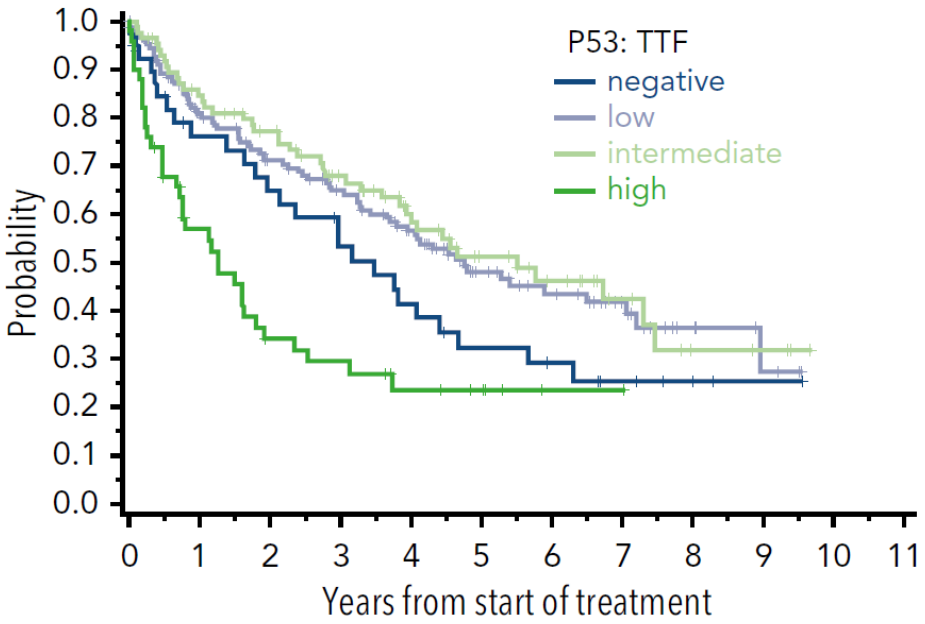


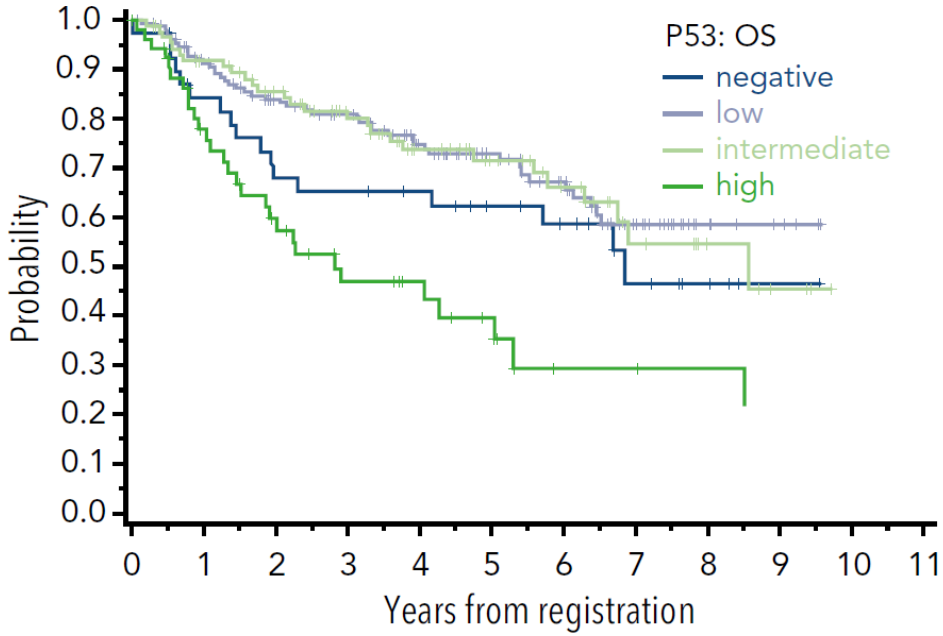


Hoster et al.

J Clin Oncol 34:1386-1394. © 2016

TP53





Expression of TP53 is associated with the outcome of MCL independent of MIPI and Ki-67 in trials of the European MCL Network

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Take-home messages

- Elevata monotonia è spesso una spia del MCL
- Alto indice di sospetto: tratto GI e tonsille
- Esistono casi con fenotipo variante
- Ki-67 rimane il fattore prognostico tissutale più importante
- A breve classificatori molecolari da FFPE